Fifty shades of chronic colitis: non-infectious imposters of inflammatory bowel disease

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Abstract

Chronic colitis is a common injury pattern that invokes a wide range of etiologic considerations. Any process that causes chronic mucosal injury can result in this nonspecific injury pattern. Inflammatory bowel disease is among the differential diagnoses, but it should only be rendered in the appropriate setting, after all possible mimics have been reasonably excluded. This review will detail the landscape of non-infectious IBD imposters.

Keywords chronic colitis; diversion colitis; diverticular disease; granulomatous disease sarcoid; inflammatory bowel disease (IBD); ischaemia; vasculitis

Introduction

The chronic colitis pattern encompasses a broad range of histomorphologic features (Box 1, Figure 1). By definition, features of chronicity must be present, but not all features are required in a single case and the individual features can be present in any proportion. For example, chronic colitis can apply to a biopsy with only focal findings, such as scattered Paneth cell metaplasia, and it can also apply to a biopsy with marked chronic changes that encompass all features presented in Box 1.

The chronic colitis pattern is one of the more treacherous areas in gastrointestinal (GI) pathology because the morphologic spectrum is broad, the underlying etiologies are diverse, and misclassification as IBD can result in potentially unnecessary immunosuppression, colectomy, and life-time surveillance. As a result, a prudent reporting approach involves describing the injury pattern in the top-line, and addressing the precise clinicopathologic context and specific etiologic considerations in the note. This approach can be time-consuming, but it will lead to optimal etiologic specific management, and minimize the potentially disastrous consequence of IBD misclassification. The most common non-infectious causes of the chronic colitis pattern are discussed below (Box 2).

Histologic features of the chronic colitis pattern

- Pyloric gland metaplasia
- Paneth cell metaplasia*
- Increased lamina propria chronic inflammation
- Architectural distortion
    - Villonodular surface
    - Abnormal crypt configuration
    - Crypt drop-out
    - Crypt shortfall (the basal crypts do not sit directly on the muscularis mucosae)
    - Basal lymphoplasmacytosis (a basal layer of lymphoplasmacytic inflammation prevents the basal crypts from sitting directly on the muscularis mucosae)

*Paneth cells are normal constituents of the right and transverse colon; their presence in the descending colon, sigmoid, and rectum is never a normal finding.

Box 1

Diverticular disease

Diverticular disease is one of the most commonly encountered IBD mimics. Colonic diverticula (singular: diverticulum) are blind mucosal outpouchings that are typically acquired secondary to the "Western" low-fibre diet. "Diverticular disease" is the broadest term that encompasses "diverticulosis" (diverticula lacking inflammation), "diverticulitis" (inflamed diverticula), and "segmental colitis associated with diverticulosis" (SCAD) syndrome (*luminal* inflammatory damage near the diverticula).

Diverticular disease is extraordinarily common in countries with low-fibre diets. These diets lead to low-bulk feces with increased transit time and increased muscle bulk and intraluminal pressures. As a result, the delicate mucosa and submucosa herniate through weaknesses in the bowel wall, particularly along the vasa recti penetration points. This close association with adjacent vessels can lead to significant gastrointestinal bleeding if the diverticulitis associated inflammation extends into the neighbouring vessels. The inflammatory damage can also result in extensive adhesive disease, abdominal pain, obstruction, and fistulization to adjacent organs. Potential triggers for diverticular disease flares include impacted fecaliths, mucosal prolapse, vascular injury, altered intestinal flora, colon dysmotility, and visceral hypersensitivity.[1–4]

In comparison to diverticulosis and diverticulitis, much less is known about the natural history of the rarely encountered SCAD syndrome. SCAD refers to inflammatory changes restricted to the *luminal* segment of colon involved by diverticular disease (there are no specific requirements for inflammatory damage within the diverticula). As with diverticulosis and diverticulitis, rectal sparing is characteristic. Some experts theorize that SCAD is a result of diverticulitis that has progressed to involve the ostia and adjacent luminal mucosa. Others suggest SCAD imparts more biologically meaningful pathology and may be an important risk factor for IBD.

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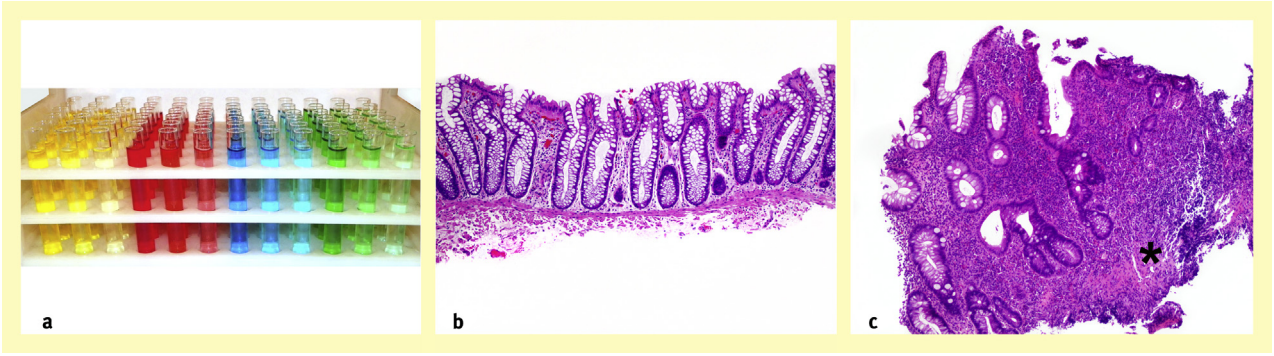

Figure 1 (**a**) Test tubes in a rack: Normal colonic architecture is analogous to test tubes in a rack, where every tube (crypt) is perfectly superimposable because they are of uniform size and separated by uniform amounts of space (lamina propria). (**b**) Normal colonic mucosa for comparison. (**c**) This example of chronic colitis features non-superimposable crypts of varying size and shape, separated by variable amounts of lamina propria. Other features of chronic colitis include a villonodular surface, the crypts fall short of the muscularis mucosae (crypt shortfall) because of the intervening basal layer of lymphocytes and plasma cells (basal lymphoplasmacytosis) (asterisk), and Paneth cell metaplasia (not seen at this power).

Endoscopically, diverticulosis appears as mucosal outpouchings lacking inflammatory injury. In contrast, both diverticulitis and SCAD involve inflammatory damage restricted to a segment of colon with diverticular disease. Histologically, the chronic colitis pattern can be seen (Figure 2a and d), and it is histologically indistinguishable from IBD. Clinicians may favour Crohn disease based on the propensity of granulomatous chronic colitis with rectal sparing.

Since up to 70% of patients over 80 years of age in the United States have diverticular disease, diverticular disease must be a top differential consideration of any biopsy in the left colon displaying chronic colitis! If diverticular disease versus IBD is the clinical question, a reasonable approach is to separately submit biopsies from the diverticular zone and uninvolved bowel segments, including the rectum. Features that favour diverticular disease include inflammatory changes confined to the segment of colon with diverticula and rectal sparing.

Top etiologic considerations of the chronic colitis pattern

- Diverticular disease
- Diversion colitis
- Therapeutics
  - NSAIDs
  - Resins
  - Ipilimumab
- Vascular injury
  - Ischaemia
  - Radiation
  - Vasculitis
- Autoimmune
  - Sarcoid
  - Common variable immunodeficiency
  - Chronic granulomatous disease
  - Vasculitis
- Infections
  - Stool pathogens
  - Cord colitis syndrome
  - Syphilitic and lymphogranuloma venereum colitis
  - Others
- Inflammatory bowel disease

Box 2

Diversion colitis

Diversion colitis is a consequence of surgical detour of a bowel segment. Surgical diversion is performed when a diseased bowel segment is removed and the remaining bowel is insufficiently long or healthy enough to immediately re-establish continuity. Generally, after the disease bowel is removed, the proximal in situ bowel segment is diverted through the anterior abdominal wall to form an ostomy site. An *ileostomy* is a diversion of the small bowel, whereas, a *colostomy* is a diversion of the colon through the anterior abdominal wall. The bowel segment downstream from the ostomy site is left in place and excluded from the fecal stream and the critical nutrients therein (specifically short-chain fatty acids).

More than 70% of patients with diversion report abdominal pain, tenesmus, rectal bleeding, and prominent rectal discharge. Endoscopic findings include mucosal friability, erosions, ulcerations, and a nodular mucosa. Corresponding histologic features include chronic colitis with florid lymphoid aggregates, conspicuous germinal centers, aphthoid lesions/ulcerations, and sometimes crypt rupture granulomata (Figure 2b and e). Diversion colitis can occur as few as 3 months following surgical diversion, and its features persist through the duration of the diversion.[5] Ostomy reversal and short-chain fatty acid enemas are curative with resolution of symptoms seen as early as 2 months.

Like all other causes of chronic colitis, diversion colitis can be histologically indistinguishable from IBD. Ulcerative colitis is a common clinical consideration because many diverted patients present with rectal bleeding and ulcerations. Useful red flags to the diagnosis of diversion colitis include any history of bowel surgery, such as diverticular disease, neoplasm, trauma, and ischaemia. Features that favour diversion colitis include