Management of Diverticular Disease in the Setting of Other Colorectal Pathology: Data on Simultaneous Issues in Segmental Colitis, Inflammatory Bowel Disease, Cancer, and Complications

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Abstract

Keywords

- acute diverticulitis
- segmental colitis associated with diverticulosis
- inflammatory bowel disease

Diverticulosis of the colon is a very common anatomical condition. In the Western world, it affects more than 70% of over 65 years old population and represents the fifth most important gastrointestinal disease in terms of health care costs in Western countries. The diagnosis of diverticular disease and diverticulitis can be challenging. Often, there is overlap with other colonic pathologies, such as segmental colitis, ischemia, inflammatory bowel disease, cancer, or infectious colitis. Management of diverticular disease in these settings might be different.

For many years, the inflammatory symptoms of the diverticular disease of the colon have been divided into two main categories:¹

1. Acute diverticulitis of the colon. This is the inflammatory process originates from the diverticula and extends to the colonic mucosa around the diverticula, but usually does not involve the interdiverticular mucosa.
2. Segmental colitis associated with diverticulosis (SCAD). This is a chronic inflammatory process localized in the colonic area presenting diverticulosis, mainly in the sigmoid colon. By definition, both the rectum and the right colon are spared from any inflammation both endoscopically and histologically.²

Recent data have hypothesized that SCAD may be an independent clinical entity within the inflammatory bowel disease (IBD) set of diseases. Several characteristics support this hypothesis:

1. Similar to IBD patients, SCAD patients present much higher levels of tumor necrosis factor- α compared with control population.³

2. Histopathology study found recently that histological inflammation was surprising similar between ulcerative colitis (UC) and SCAD, and the cytoarchitectural structure was altered in both diseases as well. However, there was mucin depletion and increased number of plasma cells, lymphocytes, and histioid cells in UC patients than in SCAD.⁴
3. In patients with SCAD refractory to conventional treatment, infliximab seems to be a good therapeutic option.⁵

Both diverticular disease and SCAD commonly affect the old population, with same colonic locations (sigmoid, descending colon) and mostly have a benign course. However, the endoscopic appearance of SCAD always shows the inflammatory involvement of the interdiverticular mucosa, with sparing of the peridiverticular mucosa and is often similar to that of IBD defined as “UC like” and “Crohn’s colitis like.”^{6,7} Histopathology is quite different between SCAD and diverticular disease. SCAD always shows active inflammatory infiltrate, often resembling UC. On the contrary, diverticular disease often shows unspecific inflammatory infiltrate, sometimes active, but never similar to that of IBD.^{8,9}

Diverticular colitis is an infrequent complication of diverticular disease. The pathogenesis of diverticular colitis (SCAD)

is likely multifactorial and includes mucosal prolapse causing relative ischemia, high exposure to intraluminal antigens and toxins, and changes in bacterial flora associated with fecal stasis. SCAD may be considered as an IBD-like inflammation occurring in the colon-harboring diverticula. Most patients with diverticular colitis respond to mesalamine oral and topical treatment, similar to the treatment for IBD. Usually, the inflammatory process has a self-limited clinical course that resolves without further recurrence or need for treatment.

For patients who fail to respond, antibiotics, probiotics, steroid enemas, or even immunosuppressive therapy may be considered. Only a minority of patients require surgical resection, which cures the disease. It should be noted that some patients with Crohn's disease or UC may initially present with features of diverticular colitis. A high level of suspicion and additional workup are warranted whether a patient diagnosed with diverticular colitis fails to improve with mesalamine treatment. It is also important to include diverticular colitis in the differential diagnosis of IBD in older patients with preexisting diverticulosis. Chronic intestinal inflammation outside the area of diverticulosis, if present, will confirm the diagnosis of Crohn's disease. However, it may be necessary to follow a patient over time before making the correct diagnosis.

Existing studies on diverticular colitis differed noticeably in case definition (inclusion/exclusion criteria and length of follow-up). Much is to be learned of this rare condition, including epidemiology, natural history, and treatment outcomes. This will likely require collaborative endeavor of multiple academic centers, so as to reach a consensus on diagnostic criteria and to assemble a large enough patient population for follow-up.¹⁰

There are numerous case reports of patients initially diagnosed with diverticular colitis who developed classic Crohn's disease or UC after surgical resection. These findings suggest that diverticular colitis may overlap with IBD in pathogenesis.¹¹

Diverticular Disease and Chronic Idiopathic Inflammatory Bowel Disease: Overlap and Association

An overlap of IBD and diverticular disease has long been recognized. Colonic diverticulosis is characterized by abnormal thickening of the bowel wall, associated with luminal overpressure and increase of sigmoid contractility. Although its association with stool consistency and thickness of the bowel wall is well established, the effect of IBD on the formation of diverticula is unclear. In fact, there are few literature data about the possible mutual interaction between IBD and diverticulosis.¹² IBD-like inflammation may occur in patients with diverticulosis and its prevalence is increasing in clinical setting.¹³

Ulcerative colitis rarely occurs in diverticulosis. In a recent prospective study, the prevalence of UC was $< 1\%$,¹⁴ which is significantly lower than SCAD prevalence in a clinical setting. Two studies approached the question of a possible mutual interaction between IBD and diverticulosis on the development and nature of inflammation. Meyers et al¹⁵ suggested

that Crohn's disease (CD) in the setting of diverticulosis may lead to the development of diverticulitis. Sultan et al¹⁶ observed an increased frequency of rectal and sigmoid inflammation, extraintestinal manifestations, and older age of IBD onset in IBD patients with diverticulosis compared with IBD patients without diverticulosis. More recent studies have found out that diverticulosis prevalence was lower in IBD (12.3%) than in the control (19.4%) group ($p < 0.001$).¹⁷ In conclusion, the prevalence of diverticulosis is lower in UC patients than in the general population. The exact mechanism responsible for this observation is yet to be assessed, but the role of chronic inflammation in determining this finding seems to be reasonable.¹²

Many of the mucosal changes in IBD are nonspecific and can be observed in other disorders with active inflammation including diverticulitis, infectious colitis, or tissues adjacent to colon cancer. The characteristic pathologic features of Crohn's disease include transmural inflammation, epithelioid cell granuloma, fissuring or fistula formation, and granulomatous cryptitis all may be seen in complicated diverticular disease or diverticulitis.¹⁸ Crohn's disease-like changes are idiosyncratic inflammatory responses to diverticulitis (rather than Crohn's disease), which may be related to bacterial stasis within the diverticula or relative ischemia. Also, some patients with well-documented diverticulitis were reported to develop extraintestinal manifestations typical of IBD, including arthritis and pyoderma gangrenosum. These patients did not respond to corticosteroids and immunosuppressive agents, but their symptoms resolved after colonic resection.¹⁰

Diverticular disease is often asymptomatic, but diverticulitis can mimic IBD, especially Crohn's disease, in the initial presentation. In such situations, a history of a prior attack of diverticulitis or IBD may help. A computed tomography (CT) scan of abdomen and pelvis with intravenous contrast is the test of choice for primary diagnosis. Unfortunately, the findings of segmental colonic thickening, pericolonic stranding, abscess, and fistula are nonspecific and can be seen in diverticulitis, Crohn's disease, and colorectal cancer. The identification of abscess or fistula guide subsequent management, but the clinician is left the task to differentiate an inflammatory versus infectious etiology. Certainly, the finding of multiple colonic diverticula in an older patient may steer the diagnosis more toward diverticulitis. Biopsies, if obtained in the acute setting, may not help as granuloma can be presented in acute diverticulitis. Response to medical therapy may not help, as both diverticulitis and Crohn's disease respond to antibiotic treatment.^{18,19}

Colonoscopy can usually differentiate diverticulitis and Crohn's disease, but it should be avoided in the acute setting to minimize the risk of perforation. In rare occasions, the distinction between diverticulitis and Crohn's colitis may not be clear until either after pathologic diagnosis of the surgical specimen or the development of Crohn's disease in other parts of the gastrointestinal tract over time. Further understanding of the overlap of IBD and diverticular disease may shed light into new therapeutic interventions.

Diverticular Disease and Colorectal Cancer: Incidental Diagnosis or Real Association?

Diverticular disease and colorectal neoplasia are common digestive disorders worldwide. Both diseases share epidemiological trends and certain risk factors including advancing age, physical inactivity, lack of dietary fibers, increased dietary saturated fats, obesity, and lifestyle. Diverticular disease, as most recent large population-based studies suggest, does not increase the risk of colon cancer after the first year of diagnosis. Within the first year of diagnosis, the association is strong, most probably due to difficulties with differential diagnosis and misclassifications and shared symptoms. All experts also agree that colon cancer has to be excluded using modern techniques after the first episode of suspected diverticulitis. In the long term, patients with colonic diverticula do not require a different follow-up for the prevention of colorectal cancer than the general population. Inflammatory polyps are frequently associated with colonic diverticular disease probably due to the same pathogenic factors.^{20–25}

The current recommendation of American Society of Colon and Rectal Surgeons include follow-up colonoscopy for the differentiation of colon cancer, ischemia, and IBDs after recovery from acute diverticulitis (typically 6 weeks after diverticulitis treatment). Abdominal CT has high specificity and sensitivity, and a low false-negative rate and so can identify complications with high precision. However, in some cases, CT cannot differentiate other abdominal inflammatory diseases, infectious diseases, or colon cancer. Mesenteric fluid collection and hyperemia of adjacent mesenteric blood vessels indicate diverticulitis when the stenosis transition is gradual, and the intestinal wall thickness is < 1 cm. Conversely, lymph node enlargement around the intestine indicates colon cancer. However, when both findings are present, differentiation of diverticulitis and colon cancer is difficult in cases in which cancer infiltration into the intestinal wall is concurrent with fat infiltration; in this situation, biopsy during colonoscopy is necessary.²⁶

In particular, colonoscopy is considered necessary if local wall thickening is observed consistently in spite of an improvement in inflammation on the follow-up CT. The importance of follow-up care should be emphasized to patients or guardians both at the time of diagnosis and during diverticulitis treatment.²⁷

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