

Segmental colitis associated diverticulosis syndrome

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Abstract

Segmental colitis associated diverticulosis (SCAD) has become increasingly appreciated as a form of inflammatory disease of the colon. Several features suggest that SCAD is a distinct disorder. SCAD tends to develop almost exclusively in older adults, predominantly, but not exclusively, males. The inflammatory

process occurs mainly in the sigmoid colon, and usually remains localized to this region of the colon alone. SCAD most often presents with rectal bleeding and subsequent endoscopic visualization reveals a well localized process with non-specific histopathologic inflammatory changes. Granulomas are not seen, and if present, may be helpful in definition of other disorders such as Crohn's disease of the colon, an entity often confused with SCAD. Bacteriologic and parasitic studies for an infectious agent are negative. Normal rectal mucosa (*i.e.*, "rectal sparing") is present and can be confirmed with normal rectal biopsies. SCAD often resolves spontaneously without treatment, or completely after a limited course of therapy with only a 5-aminosalicylate. Recurrent episodes may occur, but most often, patients with this disorder have an entirely self-limited clinical course. Occasionally, treatment with other agents, including corticosteroids, or surgical resection has been required.

Key words: Segmental colitis associated diverticulosis syndrome; Ulcerative colitis; Diverticulitis; Segmental colitis; Diverticulosis; Inflammatory bowel disease

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Core tip: Segmental colitis associated diverticulosis is an increasingly recognized inflammatory disorder involving the colon, particularly the sigmoid colon. The disorder occurs mainly in males, often presents with rectal bleeding, and endoscopic evaluation usually reveals a localized non-granulomatous process in the sigmoid colon, frequently with rectal sparing. The clinical course is generally self-limited, sometimes resolving spontaneously or responding to minimal treatment.

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INTRODUCTION

Segmental involvement of the colon with a localized inflammatory process was noted in early clinicopathological descriptions following recognition that pathological features attributed to Crohn's disease of the colon could be distinguished from those of ulcerative colitis^[1-3]. Even in some of these, however, diverticular disease, particularly in the sigmoid colon was noted. In some, Crohn's disease was considered to be a co-existent inflammatory process with sigmoid diverticulosis, particularly in elderly patients^[4]. In contrast, others believed that this form of segmental colitis with diverticulosis was a distinct form of inflammatory bowel disease^[5]. It usually occurred in the elderly with sigmoid diverticulosis, but failed to demonstrate other associated features of Crohn's disease. In addition, this form of inflammatory process often appeared to respond to drug therapy and usually had a benign clinical course^[6,7].

SEGMENTAL COLITIS ASSOCIATED DIVERTICULOSIS SYNDROME

In recent years, segmental colitis associated with diverticulosis, or segmental colitis associated diverticulosis (SCAD), has further become recognized as a distinct clinical and pathological entity. Most cases occur in males, usually following initial presentation with rectal bleeding (over 70%). Usually, the entity is almost exclusively a disorder of the elderly, often after age 50 years, and in some, referral is often made to exclude an occult colorectal malignancy^[8]. In some, diarrhea and/or abdominal pain were also present. These clinical features substantially differed from the predominately female sex distribution and younger age of patients initially diagnosed with Crohn's disease^[9] as well as in the occasionally encountered patient with Crohn's disease diagnosed after age 60 years^[10], both long-term studies from the same center. A prominent clinical feature, even in long-term follow-up studies, is responsiveness to limited treatment, often only an oral 5-aminosalicylate (5-ASA). In some, spontaneous resolution and remission without medication has been noted, even in those followed for several years. Sometimes, however, persistent chronically active and symptomatic disease developed, or recurrent separate episodes, all leading to use of corticosteroids and/or eventual surgical resection, usually of the involved sigmoid colon segment.

PATHOLOGICAL AND LABORATORY FEATURES

SCAD is pathologically defined by a non-specific segmental or localized non-granulomatous inflammatory process, usually confined to the sigmoid colon. Rectal sparing is best documented by direct macroscopic

visualization and histopathologic confirmation of normal mucosa in the rectum. Multiple diverticula are also clearly seen. An endoscopic feature of SCAD is that inflammation is detected within the inter-diverticular mucosa without necessarily involving diverticular orifices^[11] or as so-called crescentic fold disease^[12]. Similar localized changes have been reported recently with ipilimumab-associated colitis^[13]. Fever and leukocytosis are characteristically absent^[14]. Most routine laboratory studies are normal, including fecal studies for bacterial and parasitic agents. Serological markers, specifically perinuclear neutrophil cytoplasmic antibodies (*i.e.*, pANCA) and anti-Saccharomyces cerevisiae antibodies (*i.e.*, ASCA), often positive in other forms of inflammatory bowel disease including ulcerative colitis and Crohn's disease^[15], have been routinely negative^[8], while fecal calprotectin may be useful in differentiating SCAD from other healthy controls or the irritable bowel syndrome^[16].

LONG-TERM STUDIES

In a long-term study over a 20-year period^[8], over 80% (*i.e.*, 21 of 24) received oral 5-ASA (*i.e.*) medication while the others elected not to receive treatment. No patient was treated with oral or intravenous antibiotics. All subsequently had a complete clinical and pathological resolution, including those that were not treated. Over 80% (*i.e.*, 17 of 21) treated with 5-ASA developed a remission within 6 mo, but some had persistent symptoms for more than a year, and in one, recurrent episodes of pain occurred for 7 years. Some were non-compliant with prescribed 5-ASA, however, 2 eventually resolved completely while 3 others were administered added prednisone. A total of 3 eventually required an anterior resection for persistent sigmoid inflammatory stricture.

NATURAL HISTORY OF SCAD

The natural history of SCAD has also been explored^[8]. Although recurrent SCAD was documented over a year after complete clinical and pathological resolution of the first episode, over 60% of patients suffering recurrent SCAD developed their second episode of disease more than a decade after the initial clinical episode. This study group was of particular interest because of the absence of sigmoid colonic neoplasia, given the older age of this patient group. In 3, endoscopic removal of colonic adenomas had been completed before clinical presentation with rectal bleeding and SCAD detection, while 1 had an adenoma resected after diagnosis of SCAD. Two others also developed a colon cancer, one in the rectum 4 years after SCAD had resolved, and one in the cecum 9 years after SCAD had resolved. In the latter, a resection was done for an early stage lesion. Interestingly, recurrent SCAD developed 5 years later and resolved within 2 mo using 5-ASA alone. Others have also emphasized the benign nature of this

segmental inflammatory process in a similar 7-year follow-up study^[17].

CONCLUSION

This entity, SCAD, also should have a very special clinical relevance^[18] to physicians caring for patients with inflammatory bowel disease. First, long-term studies indicate that the disease appears to often be a self-limited inflammatory process that resolves without any future disease episode or requirement for ongoing treatment. Clearly, there are some similarities of SCAD to other forms of inflammatory bowel disease, particularly Crohn's colitis. Indeed, in a Dutch study, retrospective evaluation of multiple biopsies and further appreciation for the disease course resulted in definition of SCAD in an estimated 8% of cases, particularly if diverticulosis was present^[19]. As such, the implications of an inaccurate diagnosis should be clearly obvious. A case of SCAD in the sigmoid colon labeled as Crohn's disease could conceivably lead the treating physician or clinical trial investigator (in the case of new forms of therapy) to conclude that a positive outcome was treatment-related rather than related to the natural history of an otherwise benign process. Second, although some inflammation-associated changes in SCAD may be shared with other forms of inflammatory bowel disease and its treatment, including expression of tumor necrosis factor alpha and its downregulation with treatment^[20], definition of distinct or "new" inflammatory process that has the ability to resolve with complete mucosal healing suggests a critically important need to further explore the molecular events in SCAD, especially if these could lead to complete resolution or "cure" of other more commonly recognized inflammatory processes in the intestine.

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