

TEACHING CASE

“Enterocolic phlebitis” mimicking a primary tumor of the cecum – A rare presentation of an unusual entity

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Abstract

Intestinal vasculitis is an infrequent entity in the absence of systemic vasculitis or chronic inflammatory bowel disease. The primary involvement of gut restricted to mesenteric venous territory is exceedingly rare. We report a pseudotumoural lesion of the cecum caused by localized phlebitis and venulitis associated with thrombosis, with a putative immune etiology, in a young adult presenting with obstructive intestinal crisis.

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Introduction

A 29-year-old female with long-standing abdominal discomfort and cramping midabdominal pain was admitted to our hospital for sudden onset of semi-occlusive intestinal crisis without vomiting, fever, diarrhea, or blood in the stool. On physical examination, the abdomen was moderately tender at the right lower quadrant and the periumbilical area. Neither stigmata of cutaneous nor mucosal lesions suggestive of systemic vasculitis were detected on physical examination. The patient is a mild to moderate smoker, and she had been on oral estrogenic hormone therapy for contraception for more than 5 years. Other factors potentially associated with venous thrombosis were excluded. She denied taking any other drugs. Abdominal X-ray findings were not conclusive. Pelvic and abdominal ultrasound study revealed an ill-defined mass

formed by adherences of small intestinal loops to the terminal segment of the ileum associated with luminal distention, the intestinal wall being mildly increased in thickness. The clinical picture was suggestive of partial mechanical obstruction, and intussusception and volvulus were suspected. An elective right hemicolectomy was performed.

Materials and methods

Selected tissue samples were formalin fixed and paraffin embedded. Four-micrometer-thick routinely stained hematoxylin–eosin sections were microscopically evaluated by two of the authors. Immunohistochemistry was performed on 4-μm representative sections after antigen retrieval using the standard avidin–biotin immunoperoxidase detection technique and the following antisera: anti-CD20 (monoclonal, 1:2000; Dako), anti-CD3 (polyclonal, 1:300; Dako), anti-CD4 (monoclonal, 1:60; Novocastra), and anti-CD8 (monoclonal, 1:15; Novocastra). Positive controls were included in

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each slide run with satisfactory results. Clinical records were reviewed to assess the medical and surgical data and patient follow-up.

Results

The surgical specimen consisted of an 18-cm-long right hemicolectomy, with a $4.5 \times 3 \times 3$ cm partially ulcerated soft and edematous mass, with irregular borders and serosal umbilication, partially involving the ileo-cecal valve. The ileal wall was slightly thickened, and the remaining colon and the appendix were unremarkable macroscopically. Eleven lymph nodes were dissected from peri-intestinal mesenteric fat.

Histopathological examination showed mucosal erosion associated with prominent submucosal edema and ischemia, as well as inflammatory lesions affecting small- and medium-sized venous vessels, transmural in distribution but with submucosal predominance. The vasculitic lesions were present at the tumoural mass and in the remaining, grossly uninvolved colonic wall. The inflammatory cell infiltrate of the venous walls was polymorphic in composition (mature small lymphocytes, neutrophils, few eosinophils, and scattered histiocytes and giant cells), but was predominantly lymphocytic and neutrophilic.

These morphological changes were associated with signs of venous thrombosis showing different stages of organization and conspicuous foci of myointimal hyperplasia, resulting in near-complete occlusion of vascular lumina. Vasculitic lesions involving arterioles and arteries were never found, as well as granulomas (Figs. 1 and 2). The appendix presented subserosal foci with similar vascular lesions, although of much less severity. The regional lymph nodes had non-specific reactive changes.

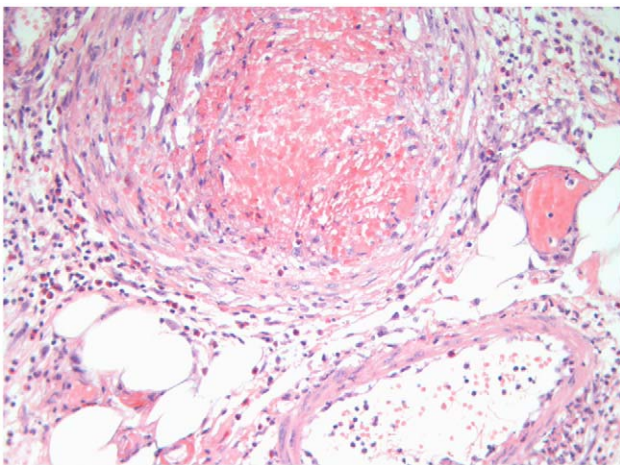


Fig. 1. Myointimal hyperplasia and lumen narrowing in a medium-sized vein with signs of recent thrombosis (hematoxylin-eosin, original magnification $\times 400$).

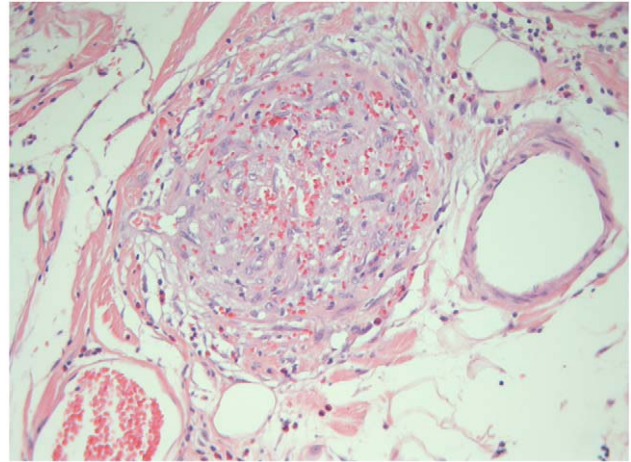


Fig. 2. Late-stage phlebitis with organized thrombosis and residual lymphocytic infiltration (hematoxylin-eosin, original magnification $\times 400$).

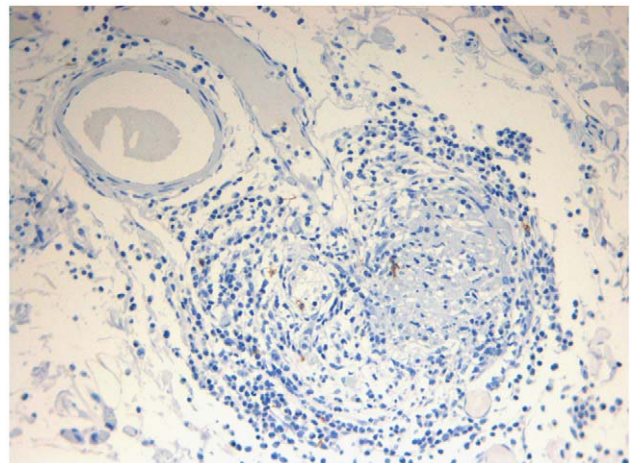


Fig. 3. CD20 immunoreactivity (original magnification $\times 400$).

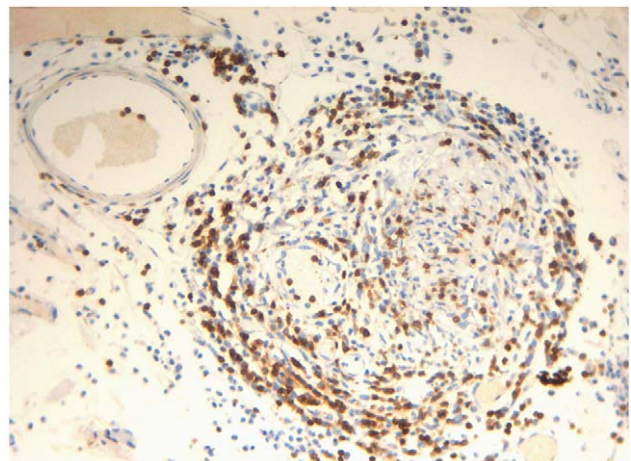


Fig. 4. CD3 immunoreactivity (original magnification $\times 400$).

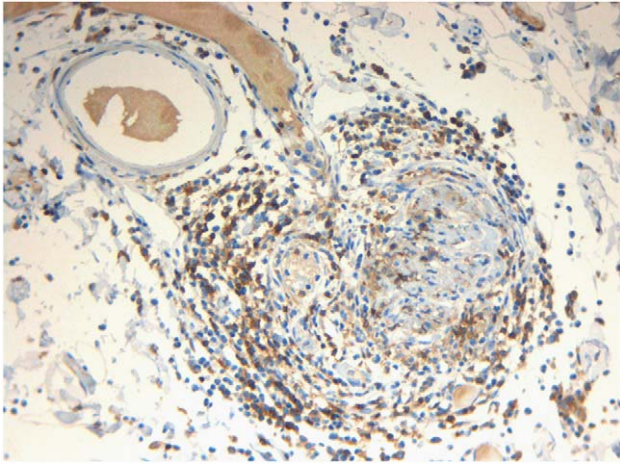


Fig. 5. CD4 immunoreactivity (original magnification $\times 400$).

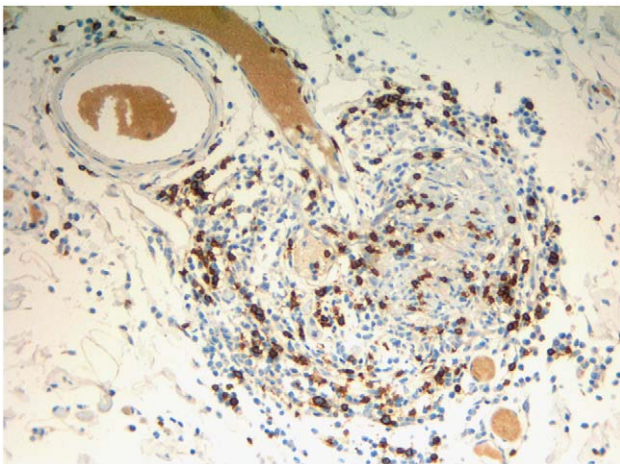


Fig. 6. CD8 immunoreactivity (original magnification $\times 400$).

Immunohistochemistry for CD20, CD3, CD4, and CD8 was performed to characterize the lymphocytic infiltrate in the venulitic lesions. Few or no B-cell lymphocytes were identified. We observed a brisk CD3-positive lymphocyte infiltrate, composed both of CD4- and CD8-positive lymphocytes, the former outnumbering the latter (Figs. 3–6).

Discussion

Vasculitis of the gastrointestinal tract has occasionally been described in systemic lupus erythematosus patients, affecting both arterioles and venules with a predominantly arteriolar involvement [6]. Examples of intestinal vasculitis have also been reported in Churg–Strauss syndrome, Behçet's disease, polyarteritis nodosa, and Henoch–Schönlein purpura, but venous inflammation is not a frequent feature of these entities [5]. Ischemic

lesions due to vasculitis limited to gastrointestinal sites have also been reported in association with Crohn's disease, and the inflammatory process also affects the arterial vasculature [1,3].

Primary intestinal phlebitis and venulitis are exceedingly rare. Very few reports received descriptive designations, namely mesenteric inflammatory veno-occlusive disease, enterocolic (lymphocytic) phlebitis, lymphocytic phlebitis, necrotizing and giant cell granulomatous phlebitis, idiopathic myointimal hyperplasia of mesenteric veins, intramural mesenteric venulitis, and idiopathic colonic phlebitis [2,4].

The larger series of this entity were reported by Flaherty et al. and Saraga et al., who described the morphologic spectrum of lesions found on surgical specimens from 13 patients, seven females and six males, aged 27–78 years. The large bowel and the small bowel were the most involved sites. Ischemic lesions associated with vasculitis and thrombosis of veins and venules with sparing of arterial tributaries were common to all cases. The vascular inflammatory infiltrate varied in composition from predominantly lymphocytic to neutrophilic with fibrin deposition (necrotizing venulitis). Granulomatous vasculitis was identified in some cases, but myointimal hyperplasia with reduction of vascular lumina was frequently present. Flaherty et al. suggested that a temporal transition from primarily necrotizing to lymphocytic inflammation may exist, and Saraga et al. hypothesized that all the cases probably belong to the same clinicopathologic entity. They suggested that thrombosis is more likely a consequence of the phlebitic and venulitic lesions and the cause of the ischemic intestinal injury. Secondary myointimal hyperplasia eventually further reduces mesenteric vascular flow and consequently contributes to increased ischemic intestinal damage [2,4]. Similarly, we identified thrombi only in inflamed veins and venules. These fibrin thrombi were found at different stages, from recent to organized, indicating a chronic pathway. Moreover, since phlebitis without thrombosis is the dominant lesion and the unaffected veins and venules did not show thrombosis, local intravascular coagulation should represent an end-stage secondary event of the chronic phlebitic and venulitic process.

The etiology of this clinicopathological entity remains to be elucidated, and no association with a definite predisposing cause was identified. A lymphocyte-mediated vascular damage linked to a hypersensitivity reaction is the most likely pathogenesis, as reported by Saraga et al. [2].

We studied the immunohistochemical profile of the lymphoid inflammatory infiltrate and, at variance with Saraga et al., who reported a mixed population of B and T-cells, we identified only T-lineage elements. CD20-positive lymphocytes were never identified in the vascular lesions. The T-cell infiltrate was composed

both of CD4-positive T helper-inducer cells and CD8-positive cytotoxic lymphocytes, with a CD4 subset predominance. Thus, our findings support Saraga's view that the vascular injury is caused by a hypersensitivity reaction, and further suggest that a delayed-type mechanism mediated by CD4 and CD8 cells might be the predominant pathogenic pathway of vein and venular injury.

Most of the patients reported by Flaherty et al. and Saraga et al. fully recovered from the surgery without any local recurrence during the follow-up. The present case illustrates an example of isolated intestinal phlebitis and venulitis with a unique presentation. The colonoscopies performed after surgery were considered normal, and the biopsies taken had mild non-specific inflammatory changes. The patient had a follow-up of 24 months, and there are neither signs of local recurrence nor evidence of extraintestinal vasculitis and inflammatory bowel disease.

To the best of our knowledge, this is the first report on a pseudotumoural clinical presentation of a primary "enterocolic phlebitis" that needs to be added to the spectrum of mass lesions of the colon occurring in

young patients without manifestations of systemic vascular disease or chronic inflammatory bowel disease.

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