Florid Vascular Proliferation of the Colon Related to Intussusception and Mucosal Prolapse: Potential Diagnostic Confusion with Angiosarcoma

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With the exception of angiodysplasia, vascular abnormalities of the intestines are unusual. We describe a florid benign vascular proliferation of the colon in five adult patients, three of whom presented with idiopathic intussusception. In all cases, the proliferation was sufficiently exuberant to raise the possibility of angiosarcoma as a diagnostic consideration. The group included 2 males and 3 females with a median age of 43 years. Two patients were HIV positive. Four patients presented with a colonic mass; other symptoms at presentation included abdominal pain, diarrhea, bleeding, and bowel obstruction. In all cases, a florid lobular proliferation of small vascular channels lined by plump endothelial cells extended from the submucosa through the entire thickness of the bowel wall. The endothelial cells showed minimal nuclear atypia, and mitotic figures were infrequent. The overlying mucosa showed ulceration with ischemic-type changes, and had features of mucosal prolapse. A possible underlying arteriovenous malformation was identified in two cases. All patients were alive and well at last follow-up (interval, 6 months to 5 years). The presence of intussusception or mucosal prolapse in all of the cases suggests repeated mechanical forces applied to the bowel wall as a possible etiologic factor. The role of HIV infection in the pathogenesis of these lesions remains to be determined.

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With the exception of angiodysplasia, vascular abnormalities of the intestines are unusual. Benign intestinal vascular lesions include telangiectasias, arteriovenous malformations, and hemangiomas (capillary and cavernous). Kaposi's sarcoma of the gastrointestinal tract occurs commonly in patients with the acquired immunodeficiency syndrome (1), whereas angiosarcoma arising in the intestines is extraordinarily rare (2–4).

Ramsden *et al.* reported a case of a florid vascular proliferation occurring in association with an ileocecal intussusception (5). The proliferation was sufficiently florid to mimic a primary angiomatous lesion. In this report, we describe a similar florid vascular proliferation of the colon in five adult patients, three of whom presented with idiopathic intussusception. In each case, the proliferation was sufficiently exuberant to raise the possibility of angiosarcoma. Based on the histologic and clinical features, we believe this process to be of a reactive rather than neoplastic nature.

METHODS

The five cases were collected from the files of the University of Michigan Department of Pathology (Cases 1 and 5), the Cleveland Clinic Foundation (Cases 2 and 3), and the University Hospitals of Cleveland (Case 4). Cases 1, 2, and 5 were seen in consultation by one of the authors (JKG, Cases 1 and 5; JRG, Case 2). Immunohistochemical staining for CD31 was performed on a Ventana 320 Automated Immunostainer (Ventana, Tucson, AZ) by

the avidin-biotin-peroxidase technique using the monoclonal antibody JC70 (DAKO; Carpinteria, CA).

RESULTS

The group of patients included 2 males and 3 females with a median age of 43 years (range, 36–82 y). Two of the patients were seropositive for the human immunodeficiency virus (HIV). The clinical characteristics of the patients are summarized in Table 1. All patients were treated by surgical resection. The follow-up interval was 6 months to 5 years (median, 6 months; mean, 23 months).

Histologic examination of each of the colonic resection specimens revealed a florid proliferation of small vascular channels arising adjacent to a chronic ulcer (Fig. 1A). The proliferation extended from the submucosa to the subserosal connective tissue. In four cases (Cases 1, 2, 4, and 5) the vessels extended into the mucosa. At low power, the lesions had a distinctly lobular architecture, similar to a pyogenic granuloma. This lobularity was accentuated on sections immunostained for CD31 (Fig. 1B). The vessels were lined by plump endothelial cells that showed strong expression of CD31 (Fig. 1, C–D). The lesions showed focal areas of increased cellularity with spindled cells (Fig. 2); however, the overall appearance was inconsistent with Kaposi's sarcoma. The endothelial cells lacked significant hyperchromasia, and nuclear pleomorphism was slight. Mitotic figures were encountered infrequently; no atypical mitoses were observed.

Muscular fibroplasia was noted in the lamina propria adjacent to the lesions, suggesting mucosal prolapse. In two of the cases (Cases 1 and 5), ischemic-type changes were present in the surrounding mucosa, including regenerative epithelium with small, atrophic crypts and hyalinization of the lamina propria (Fig. 3). A possible arteriovenous malformation (Fig. 4) was identified in two cases (Cases 3 and 5). There were no changes to suggest chronic inflammatory bowel disease, and no infectious agents were identified. A Warthin-Starry stain performed on Case 4 revealed no organisms, excluding bacillary angiomatosis.

DISCUSSION

We describe five cases of an unusual florid vascular proliferation of the colon in five adult patients. Although the etiology of the lesions is obscure, three of the patients had a documented intussusception, and all cases showed histologic evidence of mucosal prolapse. In each case, the vascular proliferation was associated with a nearby chronic ulcer. In two cases, the surrounding mucosa showed ischemic-type changes, which are known to occur in long-standing intussuseption. These findings, in conjunction with the benign nuclear features of the endothelial cells and lobularity of the lesions, suggest a reactive process. Further support for an indolent process comes from the lack of recurrence in any of the patients after resection, although the follow-up interval was relatively short in three cases.

Intussusception in children is usually idiopathic. In contrast, adult intussusception can usually be attributed to a specific cause (6–10). This tenet has recently been called into question, however, by a study in which many adult cases diagnosed using CT or magnetic resonance imaging were found to be idiopathic (11). The most common etiology of adult intussusception is the presence of a neoplasm. Other reported causes include Meckel's diverticulum, adhesions, lymphoid hyperplasia, and ectopic pancreas, among others (6–10).

There are several reports of intussusception occurring in association with vascular lesions (12–16). Most of these lesions have had the typical histologic appearance of a hemangioma. We found one report of an intussuscepting angiosarcoma (3); in contrast to our cases, this lesion was metastatic at the time of presentation. Ramsden *et al.* described a florid vascular proliferation mimicking a primary angiomatous lesion in the cecum of a patient with an ileocolic intussusception (5). The lesion consisted of closely packed, thin-walled vascular channels within the mucosa and submucosa occurring in the vicinity of a polypoid submucosal lipoma acting as a lead point to an intussusception. The mucosa adjacent to the polyp showed areas of ulceration and epithelial regeneration. In contrast to this case, our cases showed no additional mass lesion to serve as a lead point. Yao *et al.* reported three cases of

TABLE 1. Clinical Characteristics of Five Patients with Florid Vascular Proliferations of the Colon

Case	Age (y)/Sex	Site	Intussusception	Clinical Features	Follow-Up/Interval
1	82/F	Tranverse colon	No	Abdominal pain, bloody diarrhea, colonic mass	No recurrence, 5 y
2	40/F	Cecum	Yes	Abdominal pain, cecal mass	No recurrence, 6 mo
3	58/M	Cecum	Yes	Cecal mass	No recurrence, 6 mo
4	43/F	Cecum	Yes	Cecal mass, HIV+	No recurrence, 6 mo
5	36/M	Sigmoid colon	No	Diarrhea, bowel obstruction, bleeding per rectum, HIV+	No recurrence, 3 yr

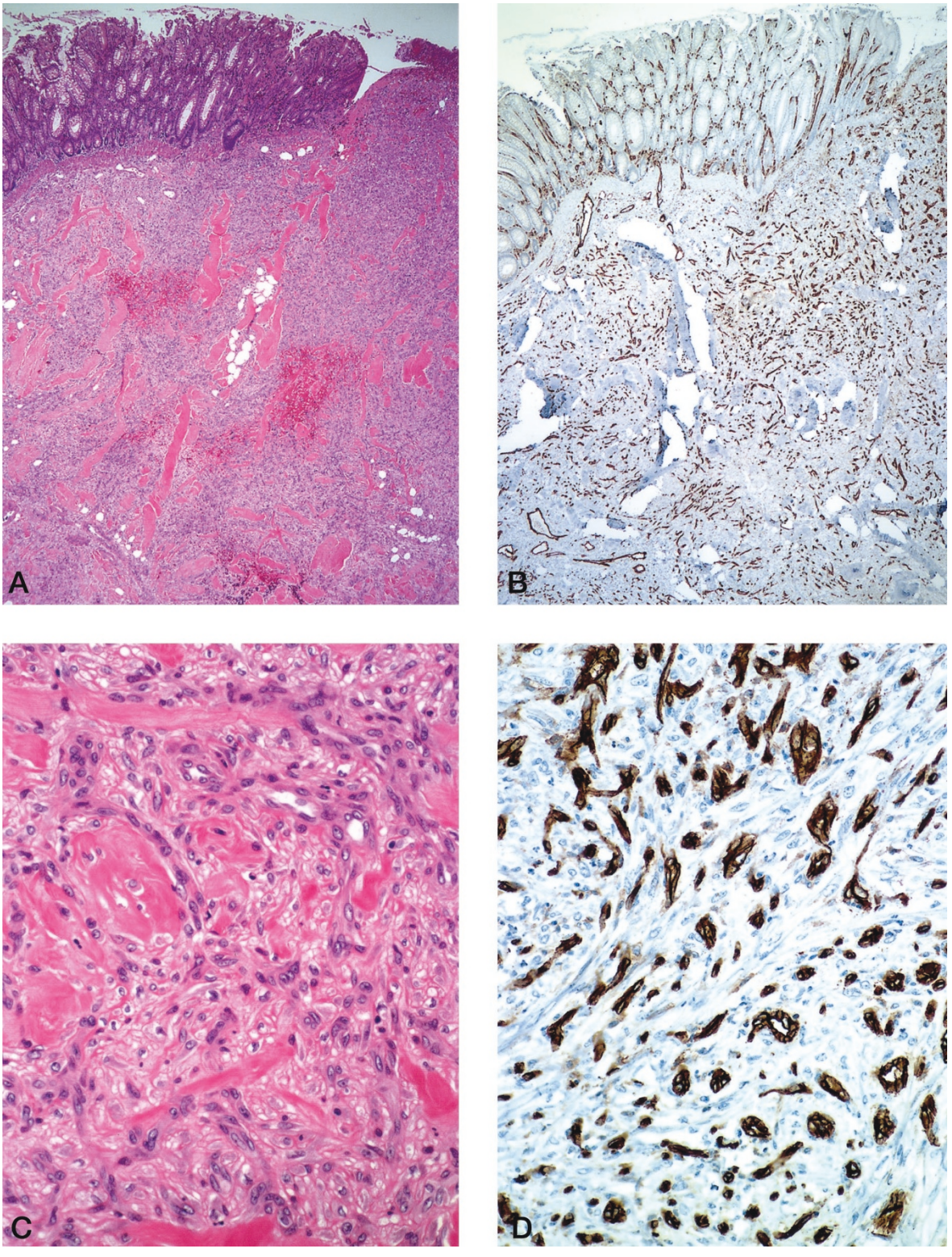

FIGURE 1. Florid vascular proliferation adjacent to chronic ulcer and extending deeply into the submucosa (**A**). Immunohistochemical stain for CD31 accentuates the lobular low-power architecture (**B**). Small vascular channels lined by bland endothelial cells (**C**) show strong expression of CD31 (**D**; Case 3).

pyogenic granuloma occurring in the intestines (17). Although our cases shared similar histologic features, they lacked the polypoid gross configuration of these lesions.

Histologic changes typically associated with intussusception include mucosal ulceration, disorganization of the muscularis propria, fusion of the muscularis mucosae with the muscularis propria,

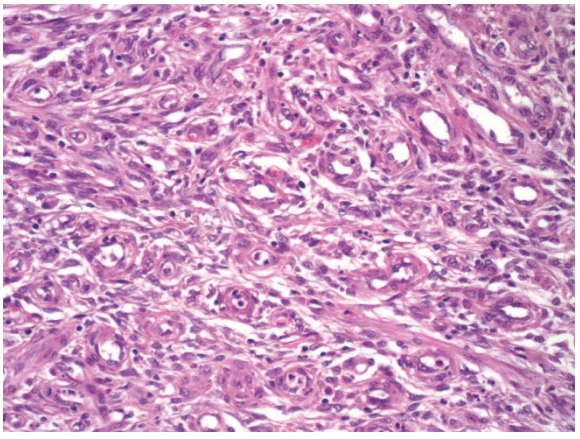

FIGURE 2. Focal area of increased cellularity and spindled cells (Case 1).

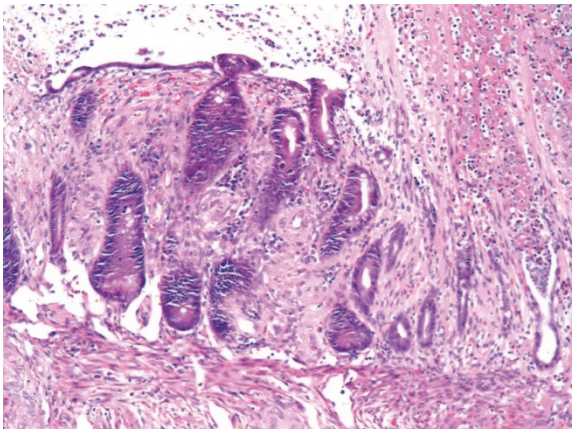

FIGURE 3. Ischemic-type changes in the mucosa adjacent to one of the lesions (Case 5).

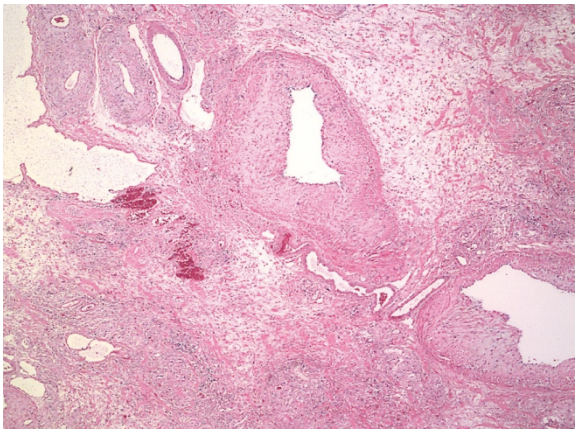

FIGURE 4. Possible arteriovenous malformation in the submucosa near one of the lesions (Case 5).

submucosal fibrosis, telangiectasia, neural hyperplasia, fibrous serosal adhesions, and mucosal hyperplasia (18). It is uncertain whether the vascular lesions we describe preceded the development of intussusception and served as a lead point or whether they resulted from longstanding mucosal prolapse associated with intussusception. It is possible that repeated mechanical forces applied to the bowel wall during prolapse or intussusception may somehow trigger angiogenesis in addition to other reactive changes. However, this hypothesis is difficult to prove. It is also possible that this process is related to the effects of repeated mechanical stress applied to a chronic ulcer, resulting in an exuberant form of highly vascularized granulation tissue.

Intussusception has been reported in adult patients with the acquired immunodeficiency syndrome, similar to two of the cases described in this report (19–27). Apparent etiologies in such cases include lymphoma (21, 23, 24, 27), mucosal lymphoid hyperplasia (26), mesenteric lymphadenopathy (28), enteric infection (20, 27, 28), and in one case, Kaposi's sarcoma (25). The relationship between HIV infection and the lesions we observed remains obscure.

In conclusion, we describe five cases of a florid vascular proliferation of the colon in which angiosarcoma was considered in the differential diagnosis. Although the pathogenesis of the lesions was unclear, there appeared to be an association with intussusception and mucosal prolapse. Consideration of this lesion may helpful in preventing the erroneous diagnosis of angiosarcoma.

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