

Estrogen- and progesterone-associated colitis: a disorder with clinical and endoscopic features mimicking Crohn's colitis

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Five women presented with episodes of abdominal pain and bloody diarrhea. Their colonic endoscopic features included (1) rectal sparing, (2) segmental involvement of the colon, and (3) discrete ulcers with normal adjacent mucosa that mimicked Crohn's colitis. All patients were taking estrogen or progesterone or both, and their symptoms and endoscopic findings resolved with cessation of therapy.

The occurrence of ischemic colitis while a patient is taking contraceptive pills has been previously reported.^{1,2} Recently we have encountered five otherwise healthy women with acute or chronic colitis whose symptoms resolved completely after cessation of estrogen or progesterone therapy. We present the clinical, endoscopic, and histological findings in these patients that are similar to, and could be mistaken for, Crohn's colitis.

CLINICAL AND LABORATORY FEATURES

The patient profiles are given in Table 1. All five patients were otherwise healthy women who presented with abdominal pain and bloody diarrhea; two had elevated temperatures. One patient had three different episodes. Stool examinations for ova, parasites, and enteric pathogens, including *Campylobacter* and *Yersinia*, were negative in all patients. The duration of hormonal therapy prior to the different episodes of symptoms varied from 1 week to 6 years. Four of the seven episodes occurred 2 to 6 years after the initiation of therapy. Patient 1 with three episodes underwent a shorter onset of symptoms after institution of therapy with each episode. The indications and hormones taken are listed in Table 1.

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ENDOSCOPIC AND RADIOLOGICAL FEATURES

The colonic abnormalities are listed in Table 2. The significant endoscopic findings included (1) rectal sparing in all patients; (2) confluent friability, erythema, and edema of the involved colonic segment (Fig. 1); and (3) discrete ulcers with normal appearing intervening mucosa of the involved colonic segments (Fig. 2). Barium enemas were obtained in all patients. These examinations were abnormal in four patients and normal in one. The abnormal features included segmental ulcerations, mucosal edema, absent haustral markings, and diffuse colonic ulcerations. Figure 3 demonstrates the finding of discrete ulcerations on the superior aspects of the transverse colon. Small bowel x-rays did not reveal any small bowel abnormalities in any patients.

CLINICAL COURSE

Patients 1 and 2 underwent exploratory laparotomy because of fever, leukocytosis, and worsening clinical findings. In both, the operative findings were consistent with a nonspecific colitis without any evidence of perforation or bowel infarction. Histological evaluation of specimens obtained by colonoscopic biopsy and surgical resection in one patient revealed mucosal inflammation without evidence of granuloma or ischemic colitis. In all patients, the clinical symptoms resolved within days to weeks after the cessation of estrogen or progesterone. The endoscopic findings and the three barium enemas that were repeated demonstrated complete resolution in all patients after

Table 1.
Patient profiles.

Patient no. ^a	Age (yr)	Hormone	Indications for hormonal therapy	Duration of hormonal therapy prior to symptoms	Duration of symptoms prior to presentation	Duration of symptom-free follow-up
1						
a	29	Norgestrel and ethinyl estradiol	Contraception	2 yr	2 yr	1.0 yr
b	31	Norethindrone and mestranol	Contraception	6 mo	2 mo	6.0 mo
c	32	Medroxyprogesterone	Irregular menses	1 wk	1 wk	4.0 mo
2	32	Estradiol (injections)	Surgical menopause	6 yrs	1 mo	2.5 yr
3	50	Conjugated estrogens (oral)	Menopause	6 mo	1 day	2.0 yr
4	25	Norethindrone and mestranol	Contraception	5 yr	5 mo	2.0 yr
5	23	Norethindrone and mestranol	Contraception	3 yr	6 wk	2.5 yr

^aLetters a, b, and c refer to the initial episode (a) and subsequent episodes (b and c) of colitis in patient 1 after restarting hormonal therapy.

Table 2.
Colonic abnormalities.

Patient no.	Location ^a	Endoscopic finding
1	(a) Cecum to descending (b) Transverse to descending (c) Transverse to descending	Confluent friability, erythema, edema Friability, erythema, edema Discrete ulcers with normal appearing intervening mucosa
2	Sigmoid	Friability, erythema, edema
3	Transverse	Friability, erythema, edema
4	Ascending to sigmoid	Discrete ulcers
5	Transverse to descending	Discrete ulcers

^aLetters a, b, and c refer to the initial episode (a) and subsequent episodes (b and c) of colitis in patient 1 after restarting hormonal therapy.

cessation of the hormonal therapy. The duration of symptom-free follow-up (Table 1) has ranged from 4 months to 2.5 years.

DISCUSSION

The diagnosis of ulcerative colitis, Crohn's colitis, and ischemic colitis usually depends upon the combination of consistent clinical, radiological, and pathological findings, as well as negative bacteriological and parasitological data. The five patients in this study presented with clinical and radiological findings that were similar to Crohn's colitis. These findings were encountered in otherwise healthy women whose symptoms resolved with cessation of estrogen or progesterone therapy. The apparent association of colonic disease with the widespread usage of oral contraceptives has been previously described. Kilpatrick et al.³ described two patients who developed bloody diarrhea and abdominal pain while taking oral contraceptives. X-rays were consistent with bowel infarction. These patients had a disappearance of their symptoms and a return to normal of their x-rays on discontinuation of their anovulatory agent. Other authors⁴ have described similar patients as well as patients with surgically confirmed gangrene of the small and large

bowels. These cases in conjunction with the described thromboses of celiac arteries, the superior and inferior mesenteric arteries, appear to establish the relationship of oral contraceptives and ischemic bowel diseases.⁵⁻⁷

Morowitz and Epstein⁸ have likewise described patients with fever, cramping abdominal pain, and rectal bleeding. Proctoscopic examination revealed edematous and granular rectal mucosa, which on biopsy revealed mucosal inflammatory infiltrate and crypt abscesses. Barium enema revealed ulcerations and loss of haustral markings over the entire colon. This picture was considered to be similar to ulcerative colitis and appeared to improve on discontinuation of oral contraceptives. More recently, Bonfils et al.⁹ described several patients with diarrhea and pancolitis. The rectum, however, was either spared or demonstrated discrete anal or rectal ulcers in two of the six described patients and none had rectal bleeding. Four of these patients were taking oral contraceptives. Morowitz and Epstein⁸ described a patient who received oral contraceptives and developed abdominal cramps, fever, and diarrhea. A barium study was performed that revealed deep ulcerations and thickening of the terminal ileum and ascending colon. These results were

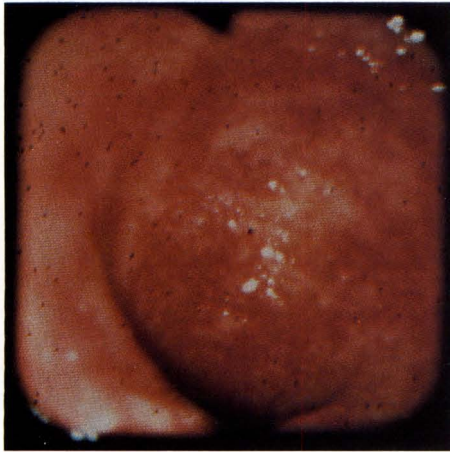


Figure 1. Endoscopic view of colon demonstrating confluent friability and erythema.



Figure 2. Endoscopic view demonstrating linear ulceration with adjacent mucosa demonstrating a normal vascular pattern.

felt to be more consistent with granulomatous ileocolitis. Discontinuation of the oral contraceptives, however, was followed by a prompt decrease in the frequency and severity of the symptoms. Gelfand¹⁰ described a patient with abdominal pain and bloody diarrhea. A barium enema was performed, revealing edema, spasm, and "thumbprinting." The patient was receiving a long acting, intramuscular synthetic progestogen medication. His paper¹⁰ suggests the possible association of colonic disease with progestogen agents as well as estrogen-containing medications. The five patients we describe were otherwise healthy women who developed acute and chronic colitis that mimicked Crohn's colitis while they were receiving estrogen or progesterone therapy.

Whether or not the common denominator in these patients with hormonal associated colitis that mimics Crohn's colitis is a decrease in mesenteric blood supply

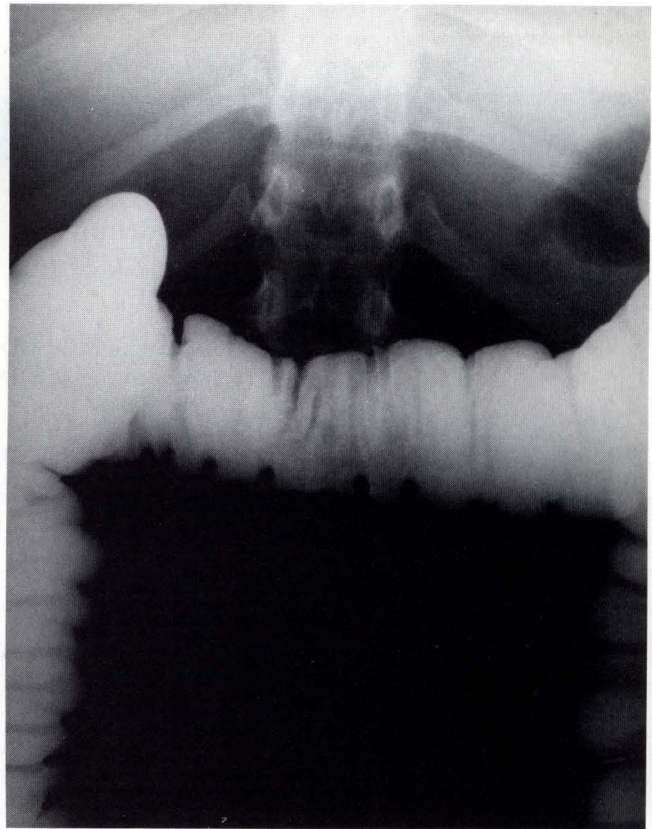


Figure 3. Barium enema demonstrating spiculation consistent with discrete ulceration on the superior aspect of the transverse colon.

remains to be further evaluated. In view of the large numbers of women taking female hormones, the association of estrogen and progesterone with colitis must be infrequent. Nevertheless, it appears reasonable to discontinue hormonal therapy in the management of patients presenting with colitis.

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