Gynecologic Aspects of Crohn's Disease

EDWARD R. FELLER, M.D., Brown Medical School, Providence, Rhode Island
SILVANA RIBAUDO, M.D., New York University School of Medicine, New York, New York
NEIL D. JACKSON, M.D., Brown Medical School, Providence, Rhode Island

Because Crohn's disease has a tendency to be transmural and to form fistulas, it may involve contiguous organs. Gynecologic involvement is frequent, diverse and often difficult to diagnose. Inflammation involving adjacent structures has been reported in as many as one third of patients. Enteric fistulas to the vagina, uterus, ovaries, perineum and vulva also have been reported. Diagnosis may not be obvious if pelvic involvement precedes active bowel disease, or if drainage is clear or mucoid. Abscesses, draining sinuses, edema and ulceration of the perineum or vulva are common, and are caused by direct extension from the involved bowel or by granulomas separated from the bowel by normal tissue. Lesions presenting with vulvar hypertrophy, a fluctuant mass or ulceration are easily misdiagnosed. Menstrual abnormalities are reported in more than one half of patients. Pelvic manifestations of Crohn's disease can be psychologically crippling. Patients or physicians may be hesitant to address serious psychosocial morbidity. To optimize management, physicians must be aware of the diverse manifestations, confusing presentations and psychologic morbidity of Crohn's disease. (Am Fam Physician 2001;64:1725-8.)

Crohn's disease is a chronic inflammatory disorder that may involve any portion of the gastrointestinal tract. Predominant symptoms of Crohn's disease include abdominal pain, diarrhea and weight loss. Because inflammation may be transmural and fistulization is frequent, involvement in any part of the female reproductive tract is possible. Complications may be the first manifestation of Crohn's disease; therefore, clinicians should be aware that unsuspected intestinal disease might be the underlying problem in women presenting with apparent gynecologic complaints. The psychosocial burden of this potentially debilitating chronic disorder has not been amply documented. This article reviews the diverse gynecologic spectrum, protean manifestations and diagnostic difficulties of pelvic Crohn's disease.

Traditional therapies, such as corticosteroids and aminosalicylates, remain effective treatment modalities. Major advances in the management of Crohn's disease (including increased use of antibiotics, immunomodulatory drugs and combination therapy, and contemporary surgical innovations) have revolutionized treatment of this chronic disease and its gynecologic complications[1] *(Table 1)*.

Abscesses, draining sinuses, edema and vulvar or perineal ulceration are common in patients with Crohn's disease.

Enteric Fistulas

Transmural inflammation penetrating directly into adjacent organs is common in Crohn's disease, and internal fistulas have been reported in as many as one third of patients[2] *(Table 2)*. In pelvic structures, enterovesical fistulas are less common in women than in men because of the anatomic position of the uterus and adnexa between the

TABLE 1
Gynecologic Complications in Crohn's Disease

Complications directly related to disease process	Complications indirectly related to disease process
Enteric fistulas from rectum, ileum, proximal colon	Anemia
Vaginal	Dysmenorrhea
Perineal	Amenorrhea
Vulvar	Malnutrition
Ovarian	Bowen's carcinoma (vulvar or vaginal)
Uterine	Pyoderma gangrenosum
Granulomatous salpingitis and oophoritis	**Iatrogenic complications**
Vulvar inflammation, abscesses, ulcerations	Perineal ulcerations and fistula formation after episiotomy
Destructive perineal disease	Corticosteroid side effects
Vaginal granulomas	**Psychosocial dysfunctioning**
	Impaired sexuality
	Poor body image
	Difficulties with socialization

TABLE 2
Mechanisms of Gynecologic Involvement in Crohn's Disease

Direct extension from diseased bowel	**Effects of chronic disease**
Transmural involvement and fistulization may affect all pelvic organs with fistulas, abscesses, edema and ulceration.	Malabsorption, malnutrition or side effects of medication may impair fertility or affect the menstrual cycle.
"Metastatic" deposits	Impaired psychosocial functioning
Granulomas or abscesses involving the perineum, vulva or vagina may form separately from diseased intestine or in the absence of active bowel disease.	The psyche, sexuality and socialization are commonly disrupted by disabling symptoms of pain and bowel or gynecologic complications, poor body image and the disfiguring reality of an ileostomy.

bowel and the bladder in women. These fistulas are associated with dysuria, pneumaturia, suprapubic pain and increased urinary frequency. In women, transmural extension of inflammation from the rectosigmoid colon to the vagina is more common.[3] If the diagnosis is unclear, polymicrobial infections or symptoms refractory to treatment may be clues to a fistula. A perirectal fistula may rupture directly into the vagina.

In a patient with longstanding active bowel inflammation and severe perianal disease who develops a fecal vaginal discharge or passage of gas vaginally, the diagnosis is apparent. However, an enterovaginal fistula may be the presenting feature of Crohn's disease and can be misdiagnosed as being the result of diverticulitis or bowel cancer. Ileal-vaginal fistulas or small fistulas with a clear discharge may not be assessed correctly or may be treated inappropriately as a primary vaginal infection. Diagnosis may be difficult. Usually, a careful examination while the patient is under anesthesia, including vaginoscopy and rectal insufflation while the vagina is filled with saline, will allow the physician to identify the fistula tract.[4] In some cases, a water-soluble rectal Gastrografin enema will demonstrate the underlying pathology. When suspected, communication may sometimes be confirmed by instilling methylene blue stain rectally and documenting dye impregnation on a previously placed vaginal tampon. A fistulogram using contrast dye or methylene blue instilled via a perineal sinus or vaginal opening may be diagnostically helpful.

Transmural intestinal inflammation from the ileum, the proximal colon or the rectum may involve any part of the female reproductive tract. Fistulas have been reported to the uterus, adnexa, vulva and perineum, as well as to the skin, umbilicus and submammary region. Patients with known inflammatory bowel disease should be questioned routinely about skin lesions, especially in the pelvis. Careful physical examination may reveal unsuspected or unmentioned cutaneous erythema, induration, ulceration or drainage.

In August 1998, an antitumor necrosis factor alpha chimeric monoclonal antibody (infliximab; Remicade), the first cytokine-targeted therapy, was approved by the U.S. Food and Drug Administration for use in patients with severe Crohn's disease. Results in patients with previously refractory enterocutaneous fistulas have reportedly been promising.[5] This agent may prove to be useful in the treatment of gynecologic fistulas in Crohn's disease.

Vulvar and Perineal Disease

Abscesses, draining sinuses, edema and vulvar or perineal ulceration are common in patients with Crohn's disease. Physicians must be aware that such involvement may precede bowel symptoms, and these conditions can be misdiagnosed. In patients with known Crohn's disease, any perineal disorder should be considered to be associated with the underlying inflammatory bowel disease. Evidence suggests that in patients with Crohn's disease, vaginal delivery with episiotomy may be associated with a high rate of subsequent perineal disease.[6] Crohn's disease should be suspected in patients whenever severe perineal disease or a rectovaginal fistula develops after vaginal delivery. In patients presenting with ulcerative vaginal lesions, a diagnosis of Crohn's disease must be considered. Excellent results treating perianal and perineal Crohn's disease have been achieved with metronidazole (Flagyl) therapy and

The Authors

EDWARD R. FELLER, M.D., is a clinical professor in the Department of Medicine at Brown Medical School, Providence, R.I., and director in the Division of Gastroenterology at Miriam Hospital, also in Providence. Dr. Feller received his medical degree from New Jersey Medical School, Newark. He completed a fellowship in gastroenterology at Massachusetts General Hospital, Harvard Medical School, Boston.

SILVANA RIBAUDO, M.D., is a third-year resident in the Department of Obstetrics and Gynecology at New York University School of Medicine, Downtown Medical Center, New York City. She received her medical degree from Brown Medical School.

NEIL D. JACKSON, M.D., is clinical professor in the Department of Obstetrics and Gynecology at Brown Medical School. Dr. Jackson received his medical degree from Boston University School of Medicine. He completed a residency in obstetrics and gynecology at the National Naval Medical Center, Bethesda, Md.

Address correspondence to Edward R. Feller, M.D., One Randall Square, Suite 305, Providence, RI 02904. Reprints are not available from the authors.

increased use of an immunomodulating therapy, including the use of mercaptopurine (Purinethol), azathioprine (Imuran) and antitumor necrosis factor.[1]

Vulvar involvement may be caused by direct extension from the involved bowel.[7,8] Rarely, vulvar granulomatous lesions caused by Crohn's disease that have no connection to the gastrointestinal tract, and ulcerations occurring secondary to pyoderma gangrenosum (a cutaneous complication of Crohn's disease) have been reported.[9] Vulvar squamous cell carcinoma has also been known to arise in such lesions.[10] These lesions may present as unilateral vulvar hypertrophy, a fluctuant vulvar mass, erythema, or draining fistulas, nodules or pustules with necrotic tissue centrally. Biopsy may be crucial to a correct diagnosis. These disorders may be confused with abscess of a Bartholin's cyst, tuberculosis, actinomycosis, lymphogranuloma venereum or metastases, or may mimic genital herpes infection.[11] Physicians must be alert to the complications of vulvar involvement; attempts to incise and drain these fistulas or skin lesions have been associated with a high risk of tissue breakdown, recurrence, delay in appropriate treatment and advancement of further disease.

Menstrual Abnormalities

In one study,[12] menstrual abnormalities (including amenorrhea, irregular menses, dysmenorrhea and menorrhagia) were reported in 58 percent of 360 women with Crohn's disease. Multiple contributing factors are likely, including the influence of chronic disease, poor nutrition and medications. Physicians should be aware that nonsteroidal anti-inflammatory drugs have, in some cases, exacerbated underlying inflammatory bowel disease.[13] These medications are commonly used to treat dysmenorrhea but should be used with caution in patients with Crohn's disease or ulcerative colitis. In some patients, differentiation of pain caused by Crohn's disease and dysmenorrhea may be impossible.

Physicians may, however, educate their patients with Crohn's disease that bowel complaints may fluctuate with the menstrual cycle. Women with Crohn's disease may experience worsening of abdominal pain and diarrhea during the premenstrual and menstrual periods of their cycle. Before considering major changes in the treatment of patients with inflammatory bowel disease, physicians must take a careful menstrual history to elicit cyclic changes in symptoms and differentiate exacerbation of intestinal disease from dysmenorrheic complaints.

An accurate diagnostic assessment is difficult because children with Crohn's disease commonly present with perineal disease as the initial clinical manifestation.

Granulomatous Salpingitis and Oophoritis

In rare instances, Crohn's disease is a cause of granulomatous lesions involving the fallopian tubes or the ovaries, usually by direct extension of the inflammatory process from the bowel.[14] These lesions commonly present with unilateral pelvic pain or a pelvic mass, and may masquerade as pelvic inflammatory disease, endometriosis, active intestinal inflammation, appendicitis, diverticulitis or primary ovarian pathology. The diagnosis of Crohn's disease should be considered when a patient presents with an adnexal mass. Computed tomographic scanning with oral contrast medium will demonstrate a thickened abnormal ileum, and barium contrast studies will document primary bowel pathology. Extensive adnexal disease may also impair fertility.

Special Problems in Children and Adolescents

Approximately 2 percent of patients with Crohn's disease present before 10 years of age, and 30 percent present between 10 and 19 years of age. Physicians may not suspect inflammatory bowel disease as a cause of gynecologic symptoms among patients younger than 19 years. In a study[15] of 230 pediatric patients with Crohn's disease, 29 percent had significant pelvic pathology.[15] Lesions include highly destructive perineal disease, complicated fistulas (rectourethroperineal, rectovaginal, rectolabial, multiple fistula draining sites) and simple perianal fistulas or abscesses. Children are less likely than adults to have fistulas, fecal incontinence or perineal disease. An inability to hold a retention enema (using 100 cm^3 of water mixed with methylene blue for enhanced visibility) may indicate fecal incontinence if the suspected diagnosis remains unclear after the history and physical examination are complete.

Growth retardation, malnutrition, and primary or secondary amenorrhea can occur and may not be appropriately diagnosed. An accurate diagnostic assessment is difficult because children with Crohn's disease commonly present with perineal disease as the initial clinical manifestation. Unless this association is recognized, physicians might fail to perform a gynecologic examination in young patients.

Psychosocial Manifestations

Pelvic manifestations of Crohn's disease may have a negative psychologic impact, such as damaged self-image, impaired sexuality and increased social dysfunction. It is important to discuss sexuality issues with these patients. Perineal pain with intercourse is common in women with a perineal fistula or abscess. Some patients complain of severe rectal pressure during intercourse or are sexually inhibited because they fear rectal incontinence.[12]

Psychosocial functioning may be impaired by poor body image, embarrassment associated with ileostomy and the debilitating effects of chronic disease. Malnutrition, side effects from medication and frequent problems with pain and diarrhea contribute to psychosocial dysfunction. Post-proctocolectomy, the anatomic position of the vagina is commonly reoriented posteriorly, which can create a predisposition to increased pooling of vaginal secretions and heavy vaginal discharge. Fecal incontinence may be caused by the following: voluminous diarrhea, the destructive effect of inflammatory bowel disease on rectal sphincter competency, active rectal or perineal Crohn's disease, and side effects of previous surgery. However, some women report enhanced social functioning after surgery, most likely because of improved health and sense of well-being.[16]

Final Comment

Health care professionals who treat women with Crohn's disease should be aware of the diverse spectrum of gynecologic disease in these patients and the inherent difficulties of accurate evaluation *(Table 3)*. It is vital that physicians remember the comforting power and practical importance of the physician/patient relationship. Even patients who are accustomed to discussing their bowel habits may never address the serious psychosocial disabilities of this chronic illness. Understanding the complex relationship between this disease and the effects it has on the patient's psyche, sexuality and socialization helps to validate the patient's complaints. Contemporary advances in medical and surgical therapy have decreased morbidity and improved prognosis in patients with Crohn's disease.

The authors indicate that they do not have any conflicts of interest. Sources of funding: none reported.

TABLE 3
Pitfalls in the Diagnosis and Management of Gynecologic Crohn's Disease

Abscesses, fistulas, vulvar disease or perineal pain may precede a diagnosis of Crohn's disease and be erroneously attributed to gynecologic disorders.
Abdominal pain, and pelvic or adnexal masses may be misdiagnosed as related to pelvic inflammatory disease or ovarian pathology.
Steroid use for active bowel disease may mask clinically relevant pelvic pathology.
Patient or physician may avoid discussions related to rectovaginal fistulas, severe perineal disease or issues of sexuality.
Psychosocial functioning, commonly impaired in patients with chronically debilitating disease, may be ignored unless specifically and deliberately addressed during medical encounters.
Pediatric patients may present with malnutrition and delayed pubertal development, raising confusion and emotional issues.

REFERENCES

1. Stein RB, Hanauer SB. Medical therapy for inflammatory bowel disease. Gastroenterol Clin North Am 1999;28:297-321.
2. Pardi DS, Tremaine WJ, Sandborn WJ, McCarthy JT. Renal and urologic complications of inflammatory bowel disease. Am J Gastroenterol 1998;93:504-14.
3. Cohen JL, Stricker JW, Schoetz DJ, Coller JA, Veidenheimer MC. Rectovaginal fistula in Crohn's disease. Dis Colon Rectum 1989;32:825-8.
4. Strong S, Fazio VW. The surgical management of Crohn's disease. In: Kirsner JB, ed. Inflammatory bowel disease. Philadelphia: Saunders, 2000:658-709.
5. Present, DH Rutgeerts P, Targan S, Hanauer SB, Mayer L, van Hogezand RA, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. N Engl J Med 1999;340:1398-405.
6. Brandt LJ, Estabrook SG, Reinus JF. Results of a survey to evaluate whether vaginal delivery and episiotomy lead to perineal involvement in woman with Crohn's disease. Am J Gastroenterol 1995;90:1918-22.
7. Cripps NP, Northover JM. Anovestibular fistula to Bartholin's gland. Br J Surg 1998;85:659-61.
8. Lavery HA, Pinkerton JH, Sloan J. Crohn's disease of the vulva—two further cases. Br J Dermatol 1985;113:359-63.
9. Borum ML, Cannava M, Myrie-Williams C. Refractory, disfiguring vulvar pyoderma gangrenosum and Crohn's disease [Letter]. Dig Dis Sci 1998;43:720-2.
10. Greenstein AJ, Gennuso R, Sachar DB, Heimann T, Smith H, Janowitz HD, et al. Extraintestinal cancers in inflammatory bowel disease. Cancer 1985;56:2914-21.
11. Kremer M, Nussenson E, Steinfeld M, Zuckerman P. Crohn's disease of the vulva. Am J Gastroenterol 1984;79:376-8.
12. Weber AM, Ziegler C, Belinson JL, Mitchinson AR, Widrich T, Fazio V. Gynecologic history of women with inflammatory bowel disease. Obstet Gynecol 1995;86:843-7.
13. Davies NM. Toxicity of nonsteroidal anti-inflammatory drugs in the large intestine. Dis Colon Rectum 1995;38:1311-21.
14. Wlodarski FM, Trainer TD. Granulomatous oophoritis and salpingitis associated with Crohn's disease of the appendix. Am J Obstet Gynecol 1975;122:527-8.
15. Markowitz J, Grancher K, Rosa J, Simpser E, Aiges H, Daum F. Highly destructive perianal disease in children with Crohn's disease. J Pediatr Gastroenterol Nutr 1995;21:149-53.
16. Yazdanpanah Y, Klein O, Gambiez L, Baron P, Desreumaux P, Marquis P, et al. Impact of surgery on quality of life in Crohn's disease. Am J Gastroenterol 1997;92:1897-900.