Cutaneous Manifestations of Crohn Disease

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KEYWORDS

• Extraintestinal manifestations • Crohn disease • Inflammatory bowel disease
• Cutaneous Crohn disease

KEY POINTS

- Cutaneous manifestations of inflammatory bowel disease (IBD) can often be the presenting sign of underlying gastrointestinal disease, and clinicians should have a low threshold to initiate evaluation for underlying gastrointestinal (GI) disease when patients present with representative skin lesions.
- In patients with known IBD, dermatologic manifestations are common, occurring in up to one-third of patients.
- Cutaneous extraintestinal manifestations are traditionally divided into 3 categories: (1) disease-specific lesions that show the same histopathologic findings as the underlying GI disease, (2) reactive lesions that are inflammatory lesions that do not share the GI pathology, and (3) associated conditions believed caused by HLA linkage phenomenon.
- For many extraintestinal manifestations, the cutaneous disease course does not always mirror the GI disease course, presenting a therapeutic challenge.
- Consultation and coordination of care with gastroenterology are essential for optimal patient benefit.

CROHN DISEASE

Introduction

Crohn disease (CD) is an inflammatory condition of the gastrointestinal (GI) tract, characterized by unpredictable periods of symptomatic relapses and remissions. The incidence of CD in the United States is approximately 3.1 to 14.6 per 100,000 person-years.[1,2] CD can affect any location in the GI tract, from the mouth to the anus, but most commonly presents in the terminal ileum (30%), colon (20%), or small bowel and colon (45%).[3] In addition, CD can affect other organs, including the eyes, skin, and liver, and joints, which are termed extraintestinal manifestations (EIMs).

Etiopathogenesis

The underlying cause of CD is not known, although several factors have been identified that contribute to disease onset.[1] These factors include genetic, microbial, environmental (smoking), immunologic, vascular, and psychosocial factors.[1,4,5] Medications such as nonsteroidal antiinflammatory drugs (NSAIDs) and oral contraceptives have also been implicated in the onset and worsening of CD, although this remains controversial.[6–8] The chronic inflammation in CD is driven by a dysregulated immune system and is dependent on both the Th-1 and Th-17 pathways.[9] Although there is a component of genetic susceptibility in the cause of CD, it

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does not follow a Mendelian inheritance pattern, and disease onset is likely triggered by exposure to 1 or more triggers in a genetically susceptible individual.[5] Most of the CD-related genes that have been found help to regulate the interaction of gut microbiota and the mucosal immune system.

Clinical Presentations

The clinical presentation of CD can be variable, although most patients present with abdominal pain, diarrhea, rectal bleeding, weight loss, fatigue, fevers, and malnutrition.[2] CD can present at any age, from pediatrics to patients in the sixth or seventh decades of life, but most commonly presents in early adulthood.[1] Complications of CD are also common, because of the transmural inflammation associated with the disease, and patients may present with symptoms caused by these complications.[2] The fibrostenotic phenotype of CD leads to the development of small bowel or colonic strictures, and patients often present with bowel obstructions. In addition, fistulae may form between the GI tract and other organs, including the bladder, skin, vagina, or other locations in the bowel. A subset of patients with CD present with perianal manifestations of the disease, including perianal fistulae and abscesses.

Diagnosis and treatment

The diagnosis of CD is made by a combination of laboratory studies, radiographic imaging, and ileocolonoscopy with biopsy.[2] Several different classes of medications are used to treat both the inflammation and symptoms associated with CD, including mesalamine products, short-term corticosteroids, immunomodulators (azathioprine, 6-mercaptopurine, methotrexate), biological therapies (infliximab, adalimumab, certolizumab pegol, natalizumab, vedolizumab), antibiotics, antidiarrheals, and bile-acid sequestrants. The goals of treatment are to achieve mucosal healing, avoid the development of complications and surgery, and to optimize quality of life. Approximately 70% of patients with CD require surgery during their lifetime, and many have postoperative recurrence and require additional surgical interventions.[2,10,11]

Systemic/Extraintestinal Associations

As mentioned earlier, multiple EIMs of CD have been described (**Table 1**).[2] Arthritis and arthralgias are most common, occurring in up to 50% of patients in some studies.[12,13] Ophthalmologic manifestations are rarely seen (<5% of cases), including episcleritis and anterior uveitis, and tend to occur when the GI disease is active.[14] Hepatobiliary abnormalities may be related either to CD itself or, often, to the medications used to treat it.[15] Common hepatobiliary manifestations of CD include granulomatous hepatitis, amyloidosis, fatty liver, pericholangitis, cholelithiasis, primary sclerosing cholangitis (PSC), portal vein thrombosis, and cholangiocarcinoma.[16] Patients with CD are also at an increased risk of developing venous thromboembolic disease, with a 3-fold higher risk than control patients.[17,18]

In addition to these EIMs, dermatologic manifestations of CD are common, occurring in up to one-third of patients; the remainder of this article is devoted to these cutaneous manifestations of CD.

CUTANEOUS MANIFESTATIONS OF CROHN DISEASE

The skin and oral mucosa represent easily accessible sites to monitor for development of EIMs of inflammatory bowel disease (IBD) and, consequently, there is a growing appreciation for the number of associated skin findings that occur. Estimates of prevalence vary widely for each EIM, but some range as high as 43% of patients, indicating that an understanding of these entities is critical to the effective care of patients with IBD in both the gastroenterology and dermatology settings.[12,19] Cutaneous lesions of IBD have traditionally been divided into 3 categories reflective of their etiopathology: (1) specific lesions (those that have the same histopathologic findings as the underlying GI disease), (2) reactive lesions (those in which the inflammatory process does not share the GI pathology), and (3) associated conditions (believed to be caused by HLA linkage phenomenon and sequelae of chronic inflammation).[20] In the current era of ever-expanding therapeutic options for IBD, some investigators have proposed a fourth category of EIMs, namely those that are therapy related. These EIMs are discussed in connection with the disease-associated conditions in light of certain skin findings that have potential overlap between these last 2 categories.

DISEASE-SPECIFIC CUTANEOUS MANIFESTATIONS

Perianal Fissures/Fistulae and Acrochordae

Perianal fissures and fistulae (**Fig. 1**) are one of the specific lesions of CD and are a commonly encountered finding in up to one-third of patients.[20] This finding is strongly associated with colonic involvement of CD compared with those patients with small bowel disease only. Chronic inflammation in the setting of fissures and fistulae promotes development of cutaneous abscesses and acrochordae.