EDUCATION PRACTICE

Management of Perianal Crohn's Disease

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Clinical Scenario

A 30-year-old man with a 2-year history of Crohn's disease (CD) involving the distal ileum and left colon is evaluated for a 2- to 3-week history of perianal pain and drainage. In the past, his disease was well controlled with oral mesalamine medications. He underwent a colonoscopy 1 month before this visit and was noted to have active proctitis for which mesalamine suppositories were started. On physical examination there is mild left lower-quadrant tenderness. Rectal examination is significant for an open fistula at 7 o'clock (posterior-right) that easily expresses purulent material with gentle pressure on the tract. Digital rectal examination is painful and shows an area of fluctuance within the anal canal posteriorly at 6 o'clock.

What is the role of magnetic resonance imaging (MRI) and endoscopic ultrasound (EUS) in this patient's management? What is the role of antibiotics, immunomodulators, or infliximab in this patient? What is the role of surgical evaluation and treatment in this patient?

The Problem

Approximately 25% of patients with CD will develop a perianal fistula during the course of their disease. The risk for developing a fistula is higher in patients with CD involving the left colon and rectum. Because these fistulas often involve the anal sphincters, they can be a source of significant morbidity. The rate of fecal incontinence in patients with perianal fistulas in CD is more than 70% in some studies. In addition, 10%–18% of patients with CD and perianal fistulas will require a proctectomy because of refractory disease or complications.

Fistulas form via 2 mechanisms. The primary cause of Crohn's perianal fistulas is the elongation of ulcers in the distal rectum, or anal fissures that extend over time secondary to the force of defecation (ie, stool is forced into the ulcer causing it to develop into a fistula over time). Fistulas also may form when anal glands that are present at the base of the anal crypts become infected.

Several classification schemes have been developed to describe the different perianal fistulas that can be present. The Park's classification system is the most precise system for describing perianal fistulas. This uses the external anal sphincter (EAS) as the central reference point. There are 5 different fistulas in this schema including intersphincteric, trans-sphincteric, suprasphincteric, extrasphincteric, and superficial fistulas. An intersphincteric fistula tracks between the internal anal sphincter and the EAS in the intersphincteric space. A trans-sphincteric fistula tracks from the intersphincteric space through the EAS. A suprasphincteric fistula leaves the intersphincteric space over the top of the puborectalis and penetrates the levator muscle before tracking down to the skin. An extrasphincteric fistula tracks outside of the EAS and penetrates the levator muscle into the rectum. Finally, a superficial fistula tracks below both the internal anal sphincter and EAS complexes. The precision of the Park's classification system helps facilitate accurate communication between the clinician and the surgeon regarding the perianal anatomy.

However, the Park's classification system does not include factors such as the presence of an abscess or fistulous connection to other structures such as the bladder or vagina. To overcome this shortcoming, an American Gastroenterological Association technical review panel on perianal CD developed a simplified but more clinically relevant approach to classifying fistulas. Fistulas are described as either simple or complex. A simple fistula is a superficial, intersphincteric, or low trans-sphincteric fistula that only has 1 opening and is not associated with an abscess and/or does not connect to an adjacent structure such as the vagina or bladder. In contrast, a complex fistula is one that involves more of the anal sphincter (ie, high trans-sphincteric, extrasphincteric,

Abbreviations used in this paper: AZA, azathioprine; CD, Crohn's disease; EAS, external anal sphincter; EUA, examination under anesthesia; EUS, endoscopic ultrasound; 6-MP, 6-mercaptopurine; MRI, magnetic resonance imaging.

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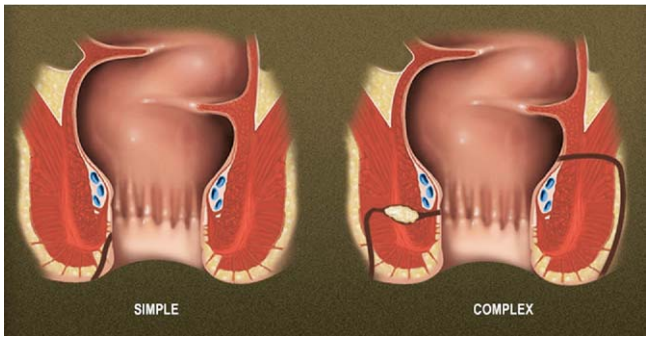

Figure 1. The diagram on the left is an example of a simple fistula. A simple fistula is a superficial, intersphincteric, or low trans-sphincteric fistula that has only one opening and is not associated with an abscess and/or does not connect to an adjacent structure such as the vagina or bladder. The diagram on the right shows examples of complex fistulas. A complex fistula is one that involves more of the anal sphincters (ie, high trans-sphincteric, extrasphincteric, or supra-sphincteric), has multiple openings, horseshoeing (crossing the midline either anteriorly or posteriorly), is associated with a perianal abscess, and/or connects to an adjacent structure such as the vagina or bladder.

or suprasphincteric), has multiple openings, horseshoeing (crossing the midline either anteriorly or posteriorly), is associated with a perianal abscess, and/or connects to an adjacent structure such as the vagina or bladder (Figure 1). Patients with complex fistulas are at increased risk for incontinence with aggressive surgical intervention and have a reduced chance for fistula healing.

Management Strategies and Supporting Evidence

Diagnostic Tests

Treatment strategies for perianal Crohn's disease rely on an accurate clinical assessment of both the degree of rectal inflammation and the perianal pathology before initiation of treatment. Several studies have shown that failure to recognize occult lesions can result in recurrent fistulas. A flexible sigmoidoscopy or colonoscopy should be performed to evaluate the degree of rectal inflammation present. Aggressive surgical intervention should not be performed on patients with active proctitis because the rate of healing has been shown to be significantly lower in these patients.

Because of the degree of rectal inflammation and scarring associated with perianal CD, digital rectal examination alone is not a reliable means of assessing perianal pathology. Computed tomography and fistulography are also too inaccurate to be of benefit in this situation. Studies addressing the accuracy of MRI and EUS in the assessment of fistulizing Crohn's disease have shown both modalities to be a reliable means of delineating perianal pathology with accuracies of around 90%. In addition, if either EUS or MRI is used in conjunction with surgical examination under anesthesia (EUA), 100% accuracy can be achieved. By using an accurate means of assessing perianal pathology such as MRI or EUS, one should be able to ensure that abscesses are drained and that fistula healing can be controlled to prevent abscess formation.

EUA involves the visual inspection (with or without anoscopy or proctoscopy), palpation, and/or passage of various probes into the fistulas while the patient is under general anesthesia. Occasionally, dilute hydrogen peroxide and/or methylene blue are used to help detect internal openings or connections to other structures. This allows a careful examination to be performed in a controlled setting with a minimum of discomfort for the patient. Therapeutic interventions can be performed at this time as well (see later).

Medical Treatment

Antibiotics. Antibiotics, the most commonly used treatment for perianal fistulas secondary to CD, are used for the treatment of any perianal sepsis that may be present, and for their anti-inflammatory properties. Uncontrolled studies have shown a reduction in fistula drainage in patients receiving metronidazole at doses of 750–1000 mg/day or ciprofloxacin at a dose of 1000–1500 mg/day. Improvement usually is seen after 6–8 weeks of treatment but fistulas commonly will re-occur once these medications are discontinued.

The purine analogs azathioprine (AZA) and 6-mercaptopurine (6-MP) have been the mainstay of maintenance therapy for perianal CD for the past 2–3 decades. Data supporting their use are derived largely from uncontrolled case series, and a meta-analysis that looked at 5 trials that examined AZA/6-MP for luminal CD but in which the details of fistula closure were described. As with luminal CD, it is important to optimize the doses of AZA and 6-MP to achieve the maximal effect. Doses of 2.0–2.5 mg/kg/day of AZA and 1.0–1.5 mg/kg/day of 6-MP have been shown to be the most efficacious.

The introduction of anti–tumor necrosis factor-α antibodies such as infliximab have changed the goal of therapy from control of fistula drainage to true fistula closure or fibrosis. The initial study looking at 3 doses of infliximab given at a dose of 5 mg/kg at 0, 2, and 6 weeks reported a fistula improvement rate of 68%, and complete fistula closure occurred in 55% of patients. The subsequent Accent II infliximab maintenance trial looking at the efficacy of infliximab in maintaining fistula healing showed that 39% of patients were able to maintain complete cessation of fistula drainage at the end of the 54-week trial. Current evidence suggests that concomitant immunosuppressive therapy for patients on