

Perianal Crohn's Disease

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ABSTRACT

Crohn's disease is commonly complicated by perianal manifestations. The surgeon plays a pivotal role in caring for these patients; a detailed history along with a thorough clinical exam provides the treating physician with invaluable information upon which to base further investigations and management decisions. Other than abscess drainage, medical management to control proximal disease often precedes any surgical attempt to cure the disease. Surgical interventions are indicated in selective patients, but are often complicated by poor wound healing and recurrences. A sizable percentage of these patients may need a proctectomy.

KEYWORDS: Crohn's disease, perianal, fistula

Objectives: Upon completion of this article, the reader should be able to evaluate and manage perianal Crohn's disease.

In the original description of regional ileitis, Crohn et al¹ stated in the clinical features of the new disease entity, "there are none of the perianal fistulae, condylomas or perirectal abscesses that characterize the complications of true colitis, for in this disease the rectum and colon are never involved." A few years later, Penner and Crohn² published an article with three case reports of patients with perianal fistulae in regional ileitis and concluded "we were struck by the frequent occurrence of fistula-in-ano as narrated by the patient in discussing past gastrointestinal disorders." They believed the incidence of perianal manifestation in regional ileitis to be ~14% and that the fistulae are best handled surgically by efforts directed to remove the primary disease.

It is now well established that Crohn's disease is commonly complicated by a variety of perianal lesions. These lesions confront the treating physician with a challenging clinical entity that can result in morbidity for the patient if not approached with vigilance. Patients

may be rendered incontinent if treated aggressively or may require a proctectomy in refractory cases.

INCIDENCE

The reported incidence of perianal Crohn's disease varies from 3.8 to 80%.³⁻⁵ The disparity is, in part, due to differences in definition. Some series include only patients treated surgically, others include all patients with perianal manifestations such as skin tags and hemorrhoids.

The incidence of perianal manifestations increase the more distal the involvement of the gastrointestinal tract. In a study by Hellers et al,⁶ perianal fistulae occurred in 12% of patients with ileal disease, 15% with ileocolonic disease, 41% with colonic disease that spares the rectum, and 92% of patients with rectal and colonic Crohn's disease. This finding was also confirmed by Williams et al⁷ who found that Crohn's colitis was associated with perianal complications in 52% of cases

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versus 14% when small bowel was the sole site of disease. In addition, they found that when an anal lesion is the manifesting sign, Crohn's disease will soon develop elsewhere in the intestine.

Perianal Crohn's disease may herald the development of intestinal manifestations by several months to several years. About two thirds of patients with perianal disease will be diagnosed with intestinal disease within 1 year, another third within 1 to 5 years, with only a few patients being diagnosed after more than 5 years.⁸ A small proportion with Crohn's disease may persist in having isolated perianal involvement.

ANATOMY

The management of perianal Crohn's disease requires a detailed grasp of perianal anatomy. Anatomic definition of the extent of the disease and its relation to the various structures is an essential prerequisite to understanding the etiology and classification of perianal fistulae and other perianal lesions. The anal canal is the terminal part of the large intestine. It is comprised of two layers of muscle: the internal anal sphincter and the external anal sphincter. The internal anal sphincter is an extension of the circular muscle of the rectum and is involuntary; the external anal sphincter is an extension of the pelvic musculature (puborectalis and levator ani) and is made of skeletal muscle. The dentate line is ~2 cm from the anal verge and correlates to the midpoint of the anal canal; it represents the transition point from rectal columnar epithelium cephalad and anal squamous epithelium caudad. The inferior rectum pleats to enter the

anal canal and forms the columns of Morgagni, which end at the dentate line. The anal crypts are at the base of the column of Morgagni. Anal glands have ducts that enter at the anal crypts. On average there are six anal glands, which occur more frequently in the anterior quadrant.

CLASSIFICATION

Multiple classification systems have been proposed attempting to stratify perianal manifestations of Crohn's disease based on severity of the disease and expected management outcomes.⁹⁻¹² The first classification based on surgical pathology was published by Hughes in 1978 (The Cardiff Classification), Hughes classified anal lesions into either primary or secondary. The former lesions are considered part of Crohn's disease (fissures and ulcers) and the latter problems arising from either infective and/or complications of the primary lesions (strictures, abscesses, fistulae, and skin tags). A clinical classification was then proposed, based on the presence of various specific types of ulceration, fistula/abscess, and/or stricture. A severity grade is given: 0 = not present, 1 = lesions of little impact associated with good prognosis, and 3 = lesions associated with greater morbidity and poor prognosis. A subsidiary classification covers associated conditions, proximal disease, and disease activity (see Table 1). Irvine¹¹ developed the Perianal Disease Activity Index (PDAI) and tested it on 37 patients at 124 office visits. Each of the five elements identified was graded on a 5-point Likert scale (Table 2). The correlation between the PDAI (max = 20 points)

Table 1 Hughes' Cardiff Classification of Anal Crohn's Disease (U.F.S.)^{9,10}

Ulceration (U.)	Fistula or abscess (F.)	Stricture (S.)
0 Not present	0 Not present	0 Not present
1 Superficial fissures	1 Low or superficial	1 Reversible stricture
(a) Posterior and/or anterior	(a) Perianal	(a) Anal canal—spasm
(b) Lateral	(b) Anovulvar/anoscrotal	(b) Low rectum—membranous
(c) With gross skin tags	(c) Intersphincteric	(c) Spasm with severe pain (no sepsis)
	(d) Anovaginal	
2 Cavitating ulcers	2 High	2 Irreversible stricture
(a) Anal canal	(a) Blind supralelevator	(a) Anal stenosis
(b) Lower rectum	(b) High direct (anorectal)	(b) Extrarectal stricture
(c) With extension to perineal skin (aggressive ulceration)	(c) High complex	
	(d) Rectovaginal	
	(e) Ileoperineal	
Subsidiary Classification		
A Associated anal conditions	P Proximal intestinal disease	D Disease activity (in anal lesions)
0 None	0 No proximal disease	1 Active
1 Hemorrhoids	1 Contiguous rectal disease	2 Inactive
2 Malignancy	2 Colon (rectum spared)	3 Inconclusive
3 Other specify	3 Small intestine	
	4 Investigation incomplete	

Table 2 Perianal Crohn's Disease Activity Index¹¹

Discharge	
No discharge	0
Minimal mucous discharge	1
Moderate mucous or purulent discharge	2
Substantial discharge	3
Gross fecal soiling	4
Pain/restriction of activities	
No activity restriction	0
Mild discomfort, no restriction	1
Moderate discomfort, some limitation activities	2
Marked discomfort, marked limitation	3
Severe pain, severe limitation	4
Restriction of sexual activity	
No restriction in sexual activity	0
Slight restriction in sexual activity	1
Moderate limitation in sexual activity	2
Marked limitation in sexual activity	3
Unable to engage in sexual activity	4
Type of perianal disease	
No perianal disease/skin tags	0
Anal fissure or mucosal tear	1
< 3 Perianal fistulae	2
> 3 Perianal fistulae	3
Anal sphincter ulceration or fistulae with significant undermining of skin	4
Degree of induration	
No induration	0
Minimal induration	1
Moderate induration	2
Substantial induration	3
Gross fluctuance/abscess	4

and the physician and patient global assessment was good. A more recent scoring system proposed by Pikarsky et al¹² is very useful because it attempts to predict the outcome following surgical intervention in patients with perianal Crohn's disease. The scoring system has correlated well with short-term outcomes of surgical intervention. Despite their ability to document the severity of the problems objectively, none of the above classification systems has gained widespread acceptance owing to their lack of impact on clinical decision-making.

DIAGNOSIS

A thorough assessment of the extent of intestinal Crohn's disease involvement as well as perianal pathology is needed before any management decisions can be taken. This evaluation usually entails a detailed history and examination, small bowel series, colonoscopy, and a combination of endorectal ultrasound (EUS) or magnetic resonance imaging (MRI) of the pelvis and/or an examination under anesthesia (EUA) (see Table 3).

Table 3 Diagnostic Assessment

General	Intestinal	Perianal
H&P	SBS	EUA
± CRP	Colonoscopy	EUS
		MRI

H&P, history and physical; CRP, c-reactive protein; SBS, small bowel series; EUA, examination under anesthesia; EUS, endorectal ultrasound; MRI, magnetic resonance imaging.

Defining the extent of disease involvement provides vital information regarding rectal involvement and other disease sites such as the small bowel that may have to be addressed before the perianal disease. Aggressive surgical intervention should be avoided in patients with active proctitis, which has been associated with poor healing rates.

Using a combination of EUA, MRI, or EUS to delineate the extent of the perianal disease process, 100% accuracy has been reported.¹³ Computed tomography (CT), which was traditionally used to evaluate fistulae, is too inaccurate to play a role in the assessment of perianal disease and fistulography. EUS and MRI have largely replaced it.

EUA involves visual inspection, palpation, and the passage of various probes into the fistulae with the patient under general anesthesia. It has the advantage of allowing any surgical intervention needed to be performed in the same setting. Diluted hydrogen peroxide injection with or without intraoperative EUS can enhance the diagnostic accuracy and help delineate fistulae with complex tracks.

MANAGEMENT

There is no cure for Crohn's disease; thus, all management decisions should be directed at offering the patient an improved quality of life. Generally, the management of perianal Crohn's disease should seek to control perineal sepsis, avoid surgery on asymptomatic lesions, avoid surgery when active rectal inflammation is present, and treat other sites of active Crohn's disease. The ultimate goal is the resolution of symptoms with minimal risk of incontinence and avoidance of proctectomy, although proctectomy may be inevitable in up to 20% of patients.⁵

The following are general principles that apply to all types of perianal disease.¹⁴

- The control of diarrhea by dietary changes and medication may reduce perianal symptoms.
- Cleansing may relieve some of the itching and pain associated with perianal lesions. Any method used is appropriate: Sitz baths or shower will both suffice.
- Barrier creams may be used to protect the perianal skin from excoriation.

PERIANAL MANIFESTATIONS OF CROHN'S DISEASE

Skin Tags

Skin tags occur in up to 37% of Crohn's disease patients.¹⁵ There are two types of skin tags that can occur.¹⁶ The first is the typical Crohn's disease skin tag, which is a large, edematous, hard, cyanotic skin tag. These skin tags arise from lymphedema secondary to lymphatic obstruction and often coexist with intestinal inflammation. Excision of these skin tags is contraindicated as poor wound healing may follow. Management should be directed at treating the intestinal disease. The second type is a flat and broad or narrow, often referred to as "elephant ear" tag; these tags are soft, painless skin tags. The latter type may interfere with personal hygiene and if extremely bothersome may be excised once active rectal inflammation has been excluded.

Hemorrhoids

Hemorrhoids occur infrequently in patients with Crohn's disease. In a study from St Mark's Hospital in the United Kingdom,¹⁷ over a 41-year period 50,000 patients were treated for hemorrhoids, only 20 of whom had Crohn's disease. The outcome of the treatment was extremely poor as 6 patients eventually required a proctectomy due to nonhealing fistulae. The authors concluded that surgical treatment of symptomatic hemorrhoids in patients with Crohn's disease is contraindicated. A more recent report¹⁸ has challenged this view and revealed that surgical management can result in a satisfactory outcome following hemorrhoidectomy for symptomatic patients. If surgical intervention for symptomatic hemorrhoids is contemplated, active inflammation in the rectum must be excluded. The role, if any, of stapled anopexy (procedure for prolapse and hemorrhoids, PPH) has not been defined.

Anal Fissure

Fissure in ano is defined as a tear or split in the distal anal canal; fissures can be acute or chronic. Chronicity is defined by both chronology and morphology; fissures must persist beyond 6 weeks to be regarded as chronic with visible transverse internal muscle fibers on exam. Associated features include sentinel pile, hypertrophied anal papilla, and a cyanotic hue to the surrounding skin.

ETIOLOGY

Idiopathic fissures are thought to be secondary to increased internal sphincter pressure and propagated by local ischemia. They are posteriorly located in over 90% of cases where the blood supply is relatively poor. In contrast to idiopathic fissures, Crohn's disease fissures

are thought to result from direct ulceration due to the disease process and may not be related to internal sphincter spasm.

CLINICAL PRESENTATION

In early studies, the clinical presentation was thought to differ from idiopathic fissures in that Crohn's fissures tend to be asymptomatic, located in aberrant locations, and are associated with other perianal conditions. Two studies have specifically addressed fissures in Crohn's disease.^{19,20} Both studies reported that the rate of symptomatic fissures is much higher than previously believed. Sweeny et al²⁰ reported that 44% of their patients were symptomatic; 85% of patients had symptoms in the study by Fleshner et al.¹⁹ The two studies confirmed the higher incidence of aberrant location compared with idiopathic fissures as well as multiplicity of fissures in the same patient. Fleshner et al were able to show that, contrary to popular belief, surgical intervention was associated with improved outcome when compared with medical management or after abdominal surgery. Factors predictive of medical treatment success were male gender, painless fissures, and acute fissures.

DIAGNOSIS

As mentioned above, a good history and physical exam is usually able to elicit the signs of perianal fissures. If pain is a prominent feature, an abscess must be excluded often by exam under anesthesia.

MEDICAL MANAGEMENT

Conservative management of fissures includes topical analgesics if pain is a prominent feature, fiber supplementation, and sitz baths.

Medical agents that have been shown to be effective in treatment of fissures include topical nitroglycerine (0.2% ointment applied twice a day [bid] or three times a day [tid] for 6 to 8 weeks), calcium channel blockers (diltiazem 2% ointment tid applied for 6 to 8 weeks), and botulinum toxin (20 units into intersphincteric groove or into the internal sphincter on either side). All these agents are thought to result in a chemical sphincterotomy allowing idiopathic fissures to heal; their role in Crohn's disease is unknown.

SURGICAL MANAGEMENT

Anal fissures are thought to spontaneously heal in 80% of cases. Patients with painful refractory fissures can in some cases undergo lateral internal sphincterotomy once sepsis has been excluded. The rate of healing following surgery is high with a low incidence of complications. Fleshner et al¹⁹ concluded that all patients with fissures in association with Crohn's disease should be medically treated. Fissures that remain unhealed have a propensity to develop into a perianal abscess or fistula or both, and proctectomy

will ultimately be required. Local anorectal procedures, particularly a lateral internal sphincterotomy should be judiciously used in patients not responding to conservative treatment. If sphincterotomy is contemplated, consideration should be given to a closed technique to limit the size of the potentially unhealed wound.

Perianal Abscess and Fistula

Perianal abscess occurs in up to 80% of patients²¹; it often leads to perianal fistula development. A fistula is defined as an abnormal communication between two epithelial surfaces, skin and anus or rectum; other organs may also be involved such as the vagina, the bladder, or the small bowel. The complexity of fistula that follows depends on the type of abscess drained.

ETIOLOGY

The etiology of Crohn's disease fistula may be similar to a cryptogenic fistula in ano where infection in an anal gland results in local sepsis and fistula formation. The fistula may also be due to the elongation of rectal ulcers in the distal rectum or due to anal fissures that extend over time secondary to the force of evacuation.

CLINICAL PRESENTATION

Patients with abscess frequently present with acute onset of pain and require urgent surgical intervention. Fistulae can present as recurrent abscesses with or without spontaneous discharge, continuous discharge, pain, and occasionally incontinence. On examination, an acute swelling, induration, and fluctuation may be noted, or the fistula tract may be seen; gentle pressure may confirm the diagnosis with purulent drainage.

CLASSIFICATION

Several classification systems for perianal fistulae have been described; the most established one is Parks' classification. Parks classified fistulae in relation to the external anal sphincter; four fistula types were described including intersphincteric, transsphincteric, suprasphincteric, and extrasphincteric.²² A more recent classification was proposed by the American Gastroenterological Association Technical Review Panel¹⁶; the system provides a simplified, more clinically relevant approach to perianal fistulae, which were classified as either simple or complex. A simple fistula is low (superficial, intersphincteric or low transsphincteric fistula), has a single external opening, and has no undrained perianal abscess. A simple fistula is confined to the anal canal; however, the presence of active rectal Crohn's disease may complicate its management. Conversely, a complex fistula is high intersphincteric or high transsphincteric or extrasphincteric or suprasphincteric origin of the fistula tract, may have multiple external openings,

may be associated with a perianal abscess, may be associated with fistulae to adjacent organs, may be associated with the presence of an anorectal stricture, and may be associated with the presence of active rectal disease. Treatment of complex fistulae carries a high risk of poor wound healing and/or incontinence.

DIAGNOSIS

Accurate diagnosis is the cornerstone of successful outcome in the treatment of perianal Crohn's disease. The fundamentals discussed above (Table 3) apply to all perianal fistulae; a thorough history and physical exam must be performed followed by assessment of the degree of active inflammation in the colon and rectum. Finally, a combination of EUA and MRI or EUA and EUS should provide the treating physician with precise definition of the nature of the perianal disease allowing for correct classification of the fistula and appropriate management decisions.

MEDICAL MANAGEMENT

There is no role for medical management in the treatment of abscesses. The primary goal in treating perianal abscesses and fistulae is to eliminate perineal sepsis and fistula tracts with the least possible risk to continence.

Once the acute sepsis has been eliminated, fistulae may be medically treated especially in the presence of active proctitis, since this results in poor wound healing, thus medical management should be initiated.

ANTIBIOTICS

Antibiotics often represent the first-line treatment for Crohn's fistulae; their mechanism of action is unknown. It is unclear whether antibiotics are effective due to their antimicrobial activity or to their proposed immunosuppressive properties. Both metronidazole and ciprofloxacin have been used for this purpose. Metronidazole was the first to be introduced based on the hypothesis that most perianal fistulae are colonized with anaerobic bacteria. This theory was recently challenged by West et al²³ who found that the predominant organisms that colonize Crohn's fistulae are gram positive, and that treatment with ciprofloxacin for 12 weeks did not change the composition of the colonization. This study lends further support to other mechanisms including the potential immunosuppressive properties of antibiotics. Only limited noncontrolled case studies have been published that have proven the efficacy of antibiotics in the treatment of perianal Crohn's disease. Treatment with antibiotics often results in short-lived results with a very high percentage of patients developing recurrent fistulae following the discontinuation of the antibiotics. Treatment with antibiotics should be continued for 3 to 4 months with strong consideration of dose reduction and discontinuation of the medication. Prolonged use

of antibiotics gives rise to resistant bacteria and does not provide a practical long-term solution for refractory fistulae.

Metronidazole is commenced at a dose of 20 mg/kg per day divided in three doses, usually 1000 to 1500 mg/day. The side effects of metronidazole include nausea, metallic taste, and peripheral neuropathy, especially paraesthesia. Side effects are often severe enough to necessitate dose reduction or discontinuation of medication. Bernstein et al²⁴ reported a series of 21 patients with perianal Crohn's disease treated with metronidazole. All patients had a clinical response with a decrease in pain and tenderness. Fifty six percent had complete healing of their perianal disease. Clinical improvement typically occurred after 6 to 8 weeks of therapy. A follow-up study²⁵ showed exacerbation of disease with dosage reduction, as well as the occurrence of paresthesia in 50% patients.

Ciprofloxacin is used at a dose of 1000 mg/day (500 mg bid); it can be used alone or in combination with metronidazole. A recent study by West et al²⁶ compared the combination of infliximab with either ciprofloxacin or placebo in 22 patients. The follow-up was short; however, at 18 weeks patients treated with ciprofloxacin tended to respond better than the placebo group (odds ratio = 2.4). The response was measured both clinically ($\geq 50\%$ reduction in the number of draining fistulae) and radiologically (utilizing three-dimensional endoanal ultrasound and hydrogen peroxide injection). Side effects from ciprofloxacin are rare, and include headache, nausea, diarrhea, and rash.

IMMUNOSUPPRESSANT MEDICATIONS

Azathioprine and 6-Mercaptopurine Randomized controlled trials addressing the effects of azathioprine (AZA) and 6-mercaptopurine (6-MP) are lacking. In a long term, randomized, double-blinded study by Present et al²⁷ 6-MP was compared with placebo in the treatment of Crohn's disease. Forty fistulae were observed in 36 patients. The drug was found to be more effective than placebo in healing fistulae (31 versus 6%), albeit 32% of patients took longer than 3 months to respond. Side effects occurred in 10% of patients and included leucopenia, bone marrow suppression, fever, nausea, pancreatitis and osteomyelitis. All adverse events were reversible by discontinuation of the medication. A meta-analysis of published studies on the value of AZA and 6-MP in treating perianal Crohn's revealed that both were associated with fistula healing in 54% of patients versus 21% of patients who received placebo.²⁸ In a retrospective analysis, Lecomte et al²⁹ studied the predictive factors of response of perianal Crohn's disease including fistulae, fissures, and strictures to 6-MP or AZA. They found that approximately one third of patients benefited from AZA or 6-MP regarding their perianal disease. Patients

40 years and older, with recent onset of perianal disease and without a fistula, responded best to treatment. No relationship was found between perianal evolution and intestinal response to AZA or 6-MP.

The initial dose for AZA is 2.0 to 3.0 mg/kg per day and that for 6-MP is 1.0 to 1.5 mg/kg per day. Regular monitoring of complete blood count and liver enzymes must be performed if these medications are commenced. Due to their prolonged onset of action these medications are often started in conjunction with other medications such as antibiotics or infliximab.

Cyclosporine and Tacrolimus Cyclosporine and tacrolimus are calcineurin inhibitors that act by inhibiting T-cell activation and interleukin- (IL-) 2 production. Both agents possess potent immunomodulating properties and have been successfully used in the prevention of solid organ rejection for decades. Multiple noncontrolled trials have documented the efficacy of cyclosporine in the treatment of perianal disease with closure rates around 90% and a rapid duration of action.³⁰ In a study by Present and Lichtiger, intravenous cyclosporine was used at a dose of 4 mg/kg per day and then converted to oral administration of 6–8 mg/kg per day; recurrence rates were high once the treatment was discontinued. Tacrolimus at a dose of 0.2 mg/kg per day was given to 20 patients with perianal fistulae in a randomized, placebo-controlled trial by Sandborn et al.³¹ The medication was given for 10 weeks with a primary goal of fistula closure of $\geq 50\%$ and maintenance of that closure for at least 4 weeks. Oral tacrolimus was found to be effective in inducing improvement in fistula drainage (43 versus 8%), but not fistula remission (10 versus 8%).

Both medications are associated with significant side effects particularly renal impairment. Patients require frequent monitoring of drug levels and renal function.

Infliximab There is evidence linking increased levels of tumor necrosis factor- α (TNF- α) produced by T-helper 1 cell to the pathogenesis of Crohn's disease. Infliximab (Remicade; Centocor, Inc., Horsham, PA) is a chimeric monoclonal antibody against TNF- α . In a double-blinded randomized controlled trial, Present et al³² compared two doses of infliximab at 5 and 10 mg at weeks 0, 2, and 6 with placebo. The primary goal was fistula closure in $\geq 50\%$ from baseline observed at two or more consecutive study visits and a secondary goal was closure of all fistulae. Sixty-eight percent of patients who received the 5 mg/kg achieved the primary goal and 55% achieved the secondary as compared with 26% and 13%, respectively, in the placebo group. Patients receiving 10 mg/kg did not have an improved response over 5 mg/kg—both had a median response time of 2 weeks. Eleven percent of patients treated with infliximab developed perianal abscesses in the course of

their treatment compared with 3% in the placebo group; it is postulated that rapid closure of the external opening before closure of the tract leads to this complication. The ACCENT 2 trial examined the role of maintenance therapy with infliximab³³; 306 patients with fistulizing Crohn's disease were treated with 5 mg/kg of infliximab at weeks 0, 2, and 6. One-hundred ninety-five (69%) responders were randomized to maintenance therapy with placebo or infliximab 5 mg/kg every 8 weeks. The median time to loss of response was 14 weeks for placebo and more than 40 weeks for infliximab, a highly significant difference. Combining infliximab with AZA or 6-MP may result in longer lasting remission and improved tolerance.³⁴

In general, once a fistula is diagnosed and sepsis is controlled, infliximab can be commenced at a dose of 5 mg/kg; it is administered on an outpatient basis in the hospital on weeks 0, 2, and 6. It is recommended that setons be removed 2 to 6 weeks (between the second and third dose) after the fistula has ceased draining. Patients who do not improve with the first two infusions are unlikely to respond after that and the treatment should be discontinued. Moreover, despite the impressive clinical healing rate reported with infliximab, complete radiological closure may not necessarily follow,^{26,35,36} calling into question whether these fistulae will eventually reopen once the treatment is discontinued.

Most reported adverse events are mild and not necessarily related to infliximab. These problems include headaches, nausea, upper respiratory tract infections, abdominal pain, and fatigue. Major side effects are rare and include pneumonia, fever, and dyspnea. There is an increased risk of opportunistic infections including miliary tuberculosis, sepsis, and *pneumocystis carinii* pneumonia. There are also reports of increased risk of lymphoma and heart failure.

A recent report³⁷ examined the role of local injection of infliximab in the treatment of perianal Crohn's disease; an attractive alternative to reduce systemic side effects. There was a good response rate and treatment was well tolerated. Local injection of infliximab adjacent to fistula tracts in Crohn's disease requires further investigation.

SURGICAL MANAGEMENT

There is no single technique that is appropriate for the treatment of all perianal Crohn's fistulae. Treatment should be individualized for each patient and based on the surgeon's experience and judgment. As with other perianal Crohn's manifestations, the surgical approach will depend on the presence of active rectal inflammation, which is associated with a very poor healing rate if aggressive surgical management is pursued.

The only universally accepted option is that patients who present with an abscess require urgent

drainage usually under general anesthesia. It can be done through an open incision, with drainage through a cruciate incision and unroofing of the abscess cavity or via insertion of a mushroom catheter and irrigation. If a fistula is detected at the time of incision and drainage, a loose draining seton should be placed. Fistulotomy of an associated low perianal fistula should not be performed in this setting because of the risk of poor wound healing.

The use of a draining seton provides many advantages. It helps control the perineal sepsis and prevents abscess recurrence in the short term. In certain circumstances, it can be a long-term solution to complex fistulae, especially if active proctitis is present. A more definitive procedure may be attempted if deemed appropriate by the treating physician and the patient. Traditional management of fistulae was to avoid fistulotomy at all cost, as John Alexander-Williams³⁸ noted, "more patients with Crohn's disease and perianal fistulae have been rendered incontinent by aggressive surgeons than by aggressive disease."

Management of perianal fistulae depends on the complexity of the fistula and its relation to the external anal sphincter. Simple fistulae as defined above can be treated safely with fistulotomy in the absence of proctitis. Williams et al³⁹ treated 41 fistulae in 33 patients with fistulotomy (17 subcutaneous, 19 intersphincteric, and 5 low transsphincteric) with 73% and 93% of the wounds healing within 3 and 6 months, respectively. Four of the 33 patients experienced a minor degree of incontinence; three patients underwent proctectomy. Similar findings have been reported by other authors.⁴⁰⁻⁴² Fistulotomy is performed under general anesthesia with the patient either in a prone jack-knife or lithotomy position, based on the location of the fistula and the surgeons' preference. A probe is then passed through the external opening into the internal opening. Once the surgeon is satisfied that minimal external anal sphincter involvement is present, the track is divided over the probe and curetted.

Complex fistulae call for a more conservative approach. Prolonged drainage with a loose seton is frequently adequate to control sepsis and allow the fistula to heal. In the presence of active rectal inflammation, a loose seton may remain in place for months, years, or even indefinitely. White et al⁴³ used indwelling seton drainage in 10 patients with complex fistulae, all cases resulted in excellent palliation obviating the need for a proximal diversion or proctectomy despite the presence of proctitis in 6 patients. Topstad et al⁴⁴ combined the use of seton drainage with infliximab and maintenance AZA or methotrexate in the treatment of fistulizing anorectal Crohn's disease. Sixty-seven percent of the patients had complete healing and 19% had partial healing. Concomitant rectovaginal fistula was a poor prognostic indicator.

Table 4 Success Rates of Advancement Flaps in the Treatment of Fistulae in Perianal Crohn's Disease

Study	Year	No. of Patients	Healed (%)	Recurrence	Proctectomy (%)
Jones et al ⁴⁷	1987	19	57.9	Not reported	5.3
Lewis et al ⁴⁸	1990	6	83	1/6	0
Makowiec et al ⁴⁹	1995	32	89	11/32	0
Joo et al ⁴⁶	1998	26	71	7/26	0
Marchesa et al ⁵⁰	1998	13	62	5/13	23

Endorectal advancement flaps have been used in the treatment of anal fistulae in the absence of active proctitis. A flap of tissue including the mucosa, submucosa, and a portion of the circular muscle is created; it should be extended proximal enough to the internal opening so that subsequent closure is tension free. The internal opening is then excised and the distal end of the flap is sutured to the cut edge of the distal rectum/anus. This technique involves no division of external sphincter muscle, providing a viable alternative to an indwelling seton in patients without proctitis. Mizrahi et al⁴⁵ reported a 60% success rate for endorectal advancement flaps; however, the recurrence rate for Crohn's fistulae was 57%. Joo et al⁴⁶ had a 64% success rate in patients with complex fistulae; the presence of concomitant small bowel disease was a predictor of poor outcome (Table 4).⁴⁶⁻⁵⁰

There are no reports specifically addressing the application of fibrin glue in the treatment of perianal Crohn's disease fistulae. The success rate for treating cryptoglandular fistulae with fibrin glue has varied in the literature from 14 to 80%. A small group of Crohn's disease fistulae was included in a recent report of fibrin glue in the treatment of complex perianal fistulae by Zmora et al.⁵¹ Two of the seven Crohn's disease fistulae treated resulted in closure of the fistula. Some of the procedures were combined with an endorectal advancement flap. The procedure is simple, reproducible, and carries very little risk of incontinence; fibrin glue instillation may safely be employed in the treatment of Crohn's disease fistulae with a moderate likelihood of a successful outcome.

The Surgisis AFP (Cook Medical, Bloomington, IN) anal fistula plug is a bioabsorbable xenograft that has been recently introduced in the treatment of complex anal fistulae. The procedure involves identifying the fistula tract, irrigating it with hydrogen peroxide, and insertion of the plug into the tract. A critical portion of the procedure is the placement of a secure suture at the internal opening with a figure-eight stitch incorporating the internal sphincter muscle with the plug. A single center experience with the fistula plug indicated a healing rate of 80% in Crohn's fistulae.⁵² Long-term follow-up as well as reproducibility of results by other centers is unknown; however, the ease of the procedure and the minimal risk to continence makes the plug a viable alternative.

Fecal diversion with a loop ileostomy or colostomy is sometimes required in severe cases of perianal disease. Diversion of the fecal stream from the rectum and the fistula may allow both the fistula and the rectum to heal and theoretically the patient to regain functional continuity of the gastrointestinal tract. Unfortunately, the majority of patients who undergo diversion never have their intestinal continuity restored.^{53,54} Rectal stricture and colonic Crohn's are factors associated with a permanent stoma.⁵⁵ A loop ileostomy is sometimes performed in combination with local perianal procedures or prior to performing a proctectomy, thus allowing the perineal sepsis to subside and improving the wound closure rate at the time of the definitive procedure.

Proctectomy is sometimes the only remaining option in the treatment of perianal Crohn's disease; the reported rate of proctectomy is 12 to 20%.⁵ Intersphincteric dissection should be performed to minimize the risk of postoperative sinuses and poor wound healing in severe perianal Crohn's disease. Rius et al⁵⁶ used gracilis transposition in patients with perineal wounds following proctectomy with encouraging results.

Many options for the treatment of perianal fistulae are associated with Crohn's disease; a logical algorithmic sequence is detailed in Fig. 1.

Rectovaginal and Anovaginal Fistula

Rectovaginal fistulae occur in 5.9 to 10% of patients.⁵ Patients with minimal symptoms or without symptoms do not require treatment.

ETIOLOGY

The etiology of rectovaginal fistulae is similar to that of perianal fistulae.

CLINICAL PRESENTATION

Symptoms include passage of gas or stool through the vagina and recurrent vaginitis.

DIAGNOSIS

Endorectal ultrasound is essential in the assessment of these fistulae. A sphincter defect if present can significantly change the operative approach.

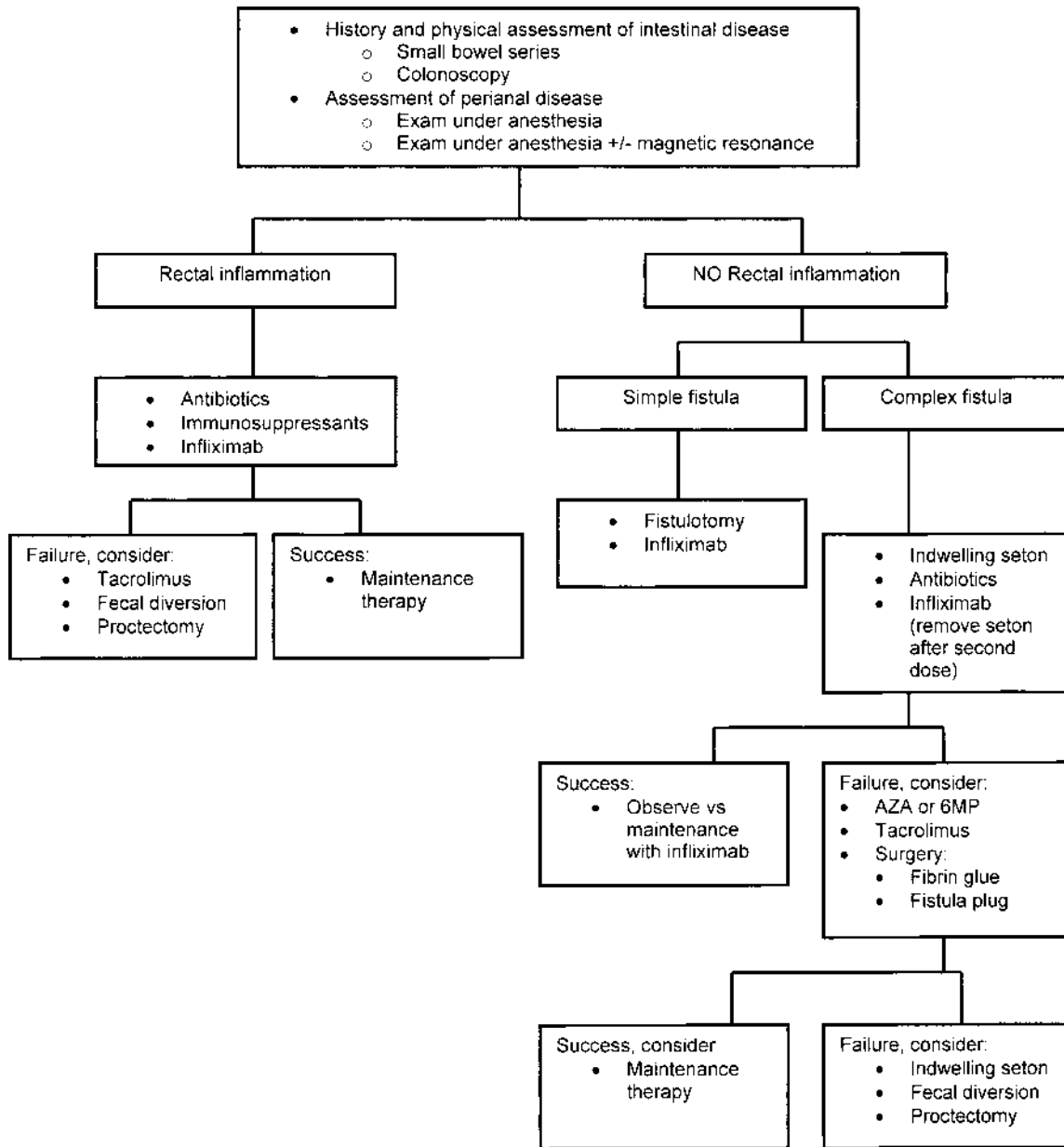


Figure 1 Treatment algorithm for perianal Crohn's disease. AZA, azathioprine; 6MP, 6 mercaptopurine.

MEDICAL MANAGEMENT

Anovaginal and rectovaginal fistulae tend to have a short and wide tract; therefore, a draining seton is not needed. In fact, the draining seton may result in enlarging the tract and should be avoided unless a septal abscess or inflammatory mass is present. The medical management follows the same guidelines as a perianal fistula.

SURGICAL MANAGEMENT

Hull and Fazio⁵⁷ used three different surgical procedures for the treatment of Crohn's fistula with an overall success rate of 70%; diverting ileostomy was performed selectively. The procedures undertaken were a curvilinear advancement rectal flap (CARF) in minimal anorectal

disease, a linear advancement rectal flap (LARF) in long and high fistulae, and an advancement sleeve flap (ASF) if there was mild rectal disease associated with severe anal ulceration. Joo et al⁴⁶ reported eradication in 75% of the rectovaginal fistulae they operated on using endorectal advancement flaps; the success rate was much higher in patients who were free of Crohn's disease in the small bowel. Sher et al⁵⁸ were able to achieve a successful outcome in 93% of patients with Crohn's colitis using a transvaginal approach. In patients with minimal rectal disease and a thin rectovaginal septum, a gracilis transposition can be used in repairing the fistulae. If a sphincter defect is present, an overlapping sphincteroplasty in combination with an advancement flap may result in an improved outcome.

Anorectal Stricture

Anal or rectal strictures may arise as complications of ulceration of the anal canal or rectum, perianal abscesses, and perianal fistulae and are often associated with ongoing rectal inflammation, complex perianal fistulae, and rectovaginal fistulae.

ETIOLOGY

Hughes¹⁰ differentiated between low rectal strictures and anal strictures based on their pathological features. In the anal canal, strictures are usually secondary to spasm; less commonly, they can be organic due to extensive sepsis. Rectal strictures are organic and of two types; the first is a membranous stricture at the anorectal junction that forms inside the lumen presumably due to circumferential ulceration. The second type is a broader extraluminal band of dense fibrous tissue, likely due to extension of a deep anal abscess.

CLINICAL PRESENTATION

Rectal strictures are either short and annular or long and tubular. Symptoms typically include urgency, tenesmus, frequency, and difficulty with evacuation.

MEDICAL MANAGEMENT

Many patients with strictures are asymptomatic and do not require any specific treatment. In the case of mild symptoms, repeated gentle dilations can be performed using a finger or Hagar dilators; this can also be done at home.

SURGICAL MANAGEMENT

Patients with severe strictures, or who fail to respond to repeat dilations, may require a proctectomy. A sleeve advancement flap has also been reported in the treatment of anal strictures that are associated with anovaginal fistulae with acceptable results.⁵⁰ Galanduik et al⁵⁵ found that the presence of a fibrotic rectal stricture was a strong indicator of the need for permanent stoma.

Cancer

Chronic perineal fistulae can undergo malignant transformation. The incidence of malignant transformation of perianal fistulae in Crohn's disease is ~0.7%.⁵⁹ Both squamous cell carcinoma and adenocarcinoma has been reported. The diagnosis may be delayed due to the difficulty in performing a thorough examination because of rectal pain and associated stricture. A high index of suspicion must be maintained in all patients with long-standing perianal fistulae; the treating physician should not hesitate to perform an exam under anesthesia with biopsies if patient discomfort precludes a thorough exam in the office. Standard oncological guidelines must be followed once a diagnosis of cancer is made.

CONCLUSION

Crohn's disease is commonly complicated by perianal manifestations. The surgeon plays a pivotal role in caring for these patients; a detailed history along with a thorough clinical exam provides the treating physician with invaluable information upon which to base further investigations and management decisions. An excellent working relationship between the gastroenterologist and the colorectal surgeon is mandatory to provide these patients with the best care possible. Other than abscess drainage, medical management to control proximal disease often precedes any surgical attempt to cure the disease. Poor wound healing and recurrences often complicate surgical interventions, culminating in a sizable percentage of these patients needing a proctectomy. Patience is a virtue in treating this condition.

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