Management of Complex Anorectal and Perianal Crohn's Disease

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Abstract

Perianal symptoms occur in up to 50% of patients with Crohn's disease in other parts of the gastrointestinal tract, and in 5% of patients it is the first manifestation of the disease. The perianal area is often under stress in patients with Crohn's disease, because of the diarrhea, and the fecal urgency, frequency, and incontinence caused by proximal disease. Symptomatic perianal disease can therefore be due to the effects of the stress on an otherwise normal anus, or the result of Crohn's disease in the low rectum and/or perianal tissues themselves. This key distinction should drive the investigation and management of anal and perianal symptoms in patients with Crohn's disease. In this review, the evaluation and management of the various manifestations of Crohn's disease in the perineum and perianal tissues will be described.

Keywords

- perianal Crohn's disease
- anorectal fistula
- anal fissure

Perianal symptoms occur in up to 50% of patients with Crohn's disease in other parts of the gastrointestinal tract, and in 5% of patients it is the first manifestation of the disease. These symptoms can be severe and can affect quality of life significantly. They are due to a collection of perianal and perineal manifestations that vary from patient to patient and call for an individualized and selective approach to their management. Some of these manifestations are secondary to the abnormal bowel habit these patients develop as a result of proximal disease and the array of surgical and medical therapies used to treat it. Other manifestations are due directly to the inflammatory sequelae of Crohn's disease, as it affects the rectum, the anus, and the perineum. Management of patients with anal and perianal symptoms centers around an accurate diagnosis of the underlying condition, identification of the manifestation causing the symptoms, and appropriate treatment chosen from a range of options. In this article, the diagnosis and management of the various manifestations of anal and perianal disease exhibited by patients with Crohn's disease will be discussed, with emphasis on the essential differentiation between patients with perineal Crohn's disease (pCD) and those without.

Perineal Crohn's Disease

In 2009, Figg and Church divided patients with perianal Crohn's disease into those with pCD and those without. The

diagnosis of pCD was based on inspection of the perineum and the finding of a waxy perineal edema with spontaneous ulceration, nonhealing perineal wounds, and painless anal fissures (►Fig. 1).¹ A more objective diagnostic criterion is the presence of Crohn's type granulomas in perineal tissues. In Figg and Church's paper, 10 of 19 patients with clinical pCD had granulomas compared with 0 of 63 patients without clinically obvious pCD. The effects of pCD on outcomes were demonstrated by the lower rate of healing (32 vs. 66%) and the higher rate of proctectomy (37 vs. 4%). In another study from the same institution, El-Gazzaz et al showed that patients with pCD as defined by the presence of perineal granulomas on biopsy responded better to biologic therapy than patients without, confirming the clinical impression described by Figg and Church.² The key data from El-Gazzaz et al are presented in ►Table 1. These are the 25 patients who had perineal granulomas on biopsy, confirming objectively the presence of pCD in all. The data are compelling, with treatment failure in 9 of 11 patients treated by surgery only and 2 of 14 patients who received biologics and surgery. Rates of proctectomy and stoma formation were also highly statistically different. This shows the importance of making the distinction between pCD and no pCD. In fact, this distinction between pCD and no pCD is at the heart of successful treatment of perianal Crohn's disease.

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Fig. 1 Perineal Crohn's disease: a fistulotomy wound over a year after it was made. There has been no healing. There are edematous tags and a painless fissure in the anus.

Table 1 Outcomes of treatment in patients with perineal Crohn's disease as defined by the presence of perineal granulomas (according to El-Gazzaz et al²)

	Surgery only	Biologics and surgery	Significance
Male/Female	8/3	10/4	ns
Length of follow-up	7 y	3 y	<0.05
Healed/improved	2 (18%)	12 (86%)	<0.05
Failed	9 (82%)	2 (14%)	<0.05
Proctectomy	8 (73%)	2 (14%)	<0.05
Stoma	9 (82%)	2 (14%)	<0.05

Manifestations of Perianal Disease in Patients with Crohn's Disease

Two recent population-based studies give an idea of the incidence of the various perianal manifestations seen in patients with Crohn's disease. They are shown in ► **Table 2**, and include strictures/stenosis, ulcers, fissures, skin tags, abscesses, and fistulas (► **Fig. 2**). Occasionally in a patient with chronic inflammation over decades, a cancer may arise in a fistula.

Assessment

History

All patients presenting with Crohn's disease should be asked about a history of anal disease and anal surgery. Symptoms to be sought include anal pain, bleeding, swelling, seepage, discharge, constipation, and incontinence. Bowel habit is documented and includes typical stool form, consistency, quantity, frequency, and urgency, as well as recent changes. A full medical history is important due to effects of many drugs on bowel habit. A history of anal surgery or the treatment of hemorrhoidal disease is asked for, and women's obstetric

Table 2 Incidence of various manifestations of perianal Crohn's disease in two population-based studies

	Peyrin-Biroulet et al ¹⁴	Eglinton et al ¹⁵
n	310	715
Time from diagnosis	10 y	9 y
Anorectal strictures	5.8%	7.4%
Anal ulcers	6.6%	
Anal fissures	10.5%	32.6%
Perianal skin tags	18.7%	11.1%
Perianal fistulas/abscess		50%/40%
Location	Olmsted County, MN	Canterbury, NZ
		Cumulative probability at 20 y of any perianal Crohn's disease was 42.7% and that of a fistula was 28.3%

Fig. 2 Perianal Crohn's disease. A 33-year-old woman with bluish colorectal of perianal skin, an anterior hooded tag concealing the internal opening of a fistula, a posterior fissure with a sentinel tag, and an abscess in the left anterior perineum.

history with details of vaginal deliveries and complications such as episiotomies or perineal tears is obtained. Patients sometimes report any or all anal symptoms as "hemorrhoids" and so it is best to keep an open mind about the diagnosis until there is a chance to look.

Examination

In asymptomatic patients, an office digital rectal examination and anoscopy is performed. Inspection looks for the classical findings of a bluish tinge to the perianal skin, the edematous "elephant ear" tags, waxy edema of the perianal skin, ulcerations, scarring, and the state of the anal sphincters (patulous

anus vs. normal vs. tight; ►Fig. 2). Perianal scarring due to hidradenitis can be noted and active hidradenitis is sometimes seen. Previous work by Church et al has established a connection between perianal hidradenitis and Crohn's disease.³ There may be incidental independent conditions such as prominent external hemorrhoidal cushions or skin irregularities from hemorrhoidal crises and treatments in the past. A gentle digital rectal examination reveals anal stenosis, the status of the anal sphincters, and the presence of any mass lesion.⁴ If a stenosis and acute sepsis is excluded, anoscopy can be performed to show the status of the anoderm, the internal hemorrhoids, and the low rectum. Sometimes, a pediatric anoscope must be used to allow anoscopy in patients with anal stenosis or a sensitive anal canal.

When patients complain of anal pain, inspection may show one or more fissures, abscesses, or fistulas (►Fig. 2). The perianal area may be asymmetric due to swelling, and may show signs of cellulitis. More detailed examination is better performed under anesthetic, where anoscopy can be comfortably done and sepsis drained.

Examination under Anesthetic

The patient is placed in lithotomy position with the buttocks overhanging the end of the table. The perianal area and anus are closely inspected for color, irregularities, and asymmetry. Skin tags, fissures, abscesses, and external fistula openings are usually obvious.

A gentle exploratory digital exam can be followed by anoscopy. The dentate line is inspected to look for the internal openings of a fistula. A bead of pus at the opening of an anal crypt can give this away. The state of the anoderm and low rectal mucosa is noted and ulcers are biopsied. External openings and sinuses are then carefully probed to look for tracks to the anus. Superficial sinuses are often due to hidradenitis. Such sinuses will not connect with the dentate line. If there is significant perineal and perianal sepsis, it is drained. Cavities are drained with mushroom catheters and sinuses/fistulas with setons. Minimize incisions unless pCD can be confidently excluded.

One of the main points of the examination under anesthesia is to make a determination about the presence of pCD (►Fig. 1). In patients with a suggestive appearance of the perineum, biopsies are taken to look for granulomas.

The Proximal Bowel

The state of the proximal bowel is relevant to the course of perianal disease. Untreated ileitis or proctocolitis causes diarrhea and stool frequency, and poor nutrition can exacerbate anal symptoms. In addition, an ulcerated anoderm prevents advancement flap repair of anal fistulas. Bowel preparation for colonoscopy in a patient with active, symptomatic anal Crohn's disease is hard to tolerate and so CT enterography is a better choice to work up the proximal bowel.

Diagnosis

Ninety-five percent of patients with perianal Crohn's disease have already been diagnosed with Crohn's because of their proximal disease. Only 5% of patients initially present with perianal Crohn's disease. Causes for suspicion include the

bluish coloration of perianal tissues; elephant ear tags; hooded tags that cover an underlying fistula; painless fissures; anal fistulas with eccentric, multiple openings; and longitudinal ulcerations in the anoderm (►Fig. 2). Failure of an apparent cryptoglandular fistula repair does not automatically mean that the diagnosis is Crohn's disease. On the other hand, biopsy of perianal and anorectal ulcers, tags, or fistulas shows typical noncaseating granulomas in only approximately 30% of cases; so, lack of pathognomic findings for Crohn's on biopsy is not necessarily a true negative. In clinically convincing, granuloma-negative cases, biologic treatments can be used empirically.

Management of Perianal Disease in Patients with Crohn's Disease

Management depends on the particular manifestation that has been seen/diagnosed:

- i. Skin tags: Skin tags are common in patients with Crohn's disease and are rarely symptomatic. Sometimes they are indicators of other perianal conditions, such as the hooded tag covering the opening of a fistula, and the sentinel tag as a sign of a fissure (►Fig. 2). If tags are causing symptoms they can be excised, as long as the patient has no active pCD. Ideally, tags are excised without preoperative infiltration of local anesthetic, as the fluid expands and distorts the base of the tag and makes accurate excision difficult. Large elephant ear tags are usually indicators of perineal Crohn's and should not be excised until the disease is well controlled by biologics.
- ii. Anal fissures: Painful anal fissures usually occur in patients with a normal anus and are due to the diarrhea caused by the proximal disease. The pathophysiology is similar to common fissures—internal sphincter spasm caused by exposure of the sphincter by the split of the anoderm. Patients with Crohn's disease may be predisposed to the split by their frequent bowel movements. Medical treatment of the fissure included agents to relax the anal sphincter (local nitrous oxide donors or calcium channel inhibitors (nitroglycerine ointment, nifedipine, diltiazem), treatment aimed at symptoms (local heat and local anesthesia), and measures to treat the diarrhea (treat the proximal Crohn's disease, loperamide, fiber supplements). If conservative treatment is ineffective, then lateral internal anal sphincterotomy can be considered. The sphincter is divided for the length of the fissure only.

Painless anal fissures are a sign of pCD. No surgery should be done on these patients. Rather, therapy with a biologic agent should be started.
- iii. Anal stenosis: Anal stenosis presents with difficult, often painful, defecation, which is often precipitated by a stool becoming more formed as proximal disease responds to therapy. The diagnosis is best confirmed by an examination under anesthetic (EUA), because inspection of the anal canal requires an initial dilation. There are at least four different causes for anorectal stenosis in the setting of Crohn's disease.

- a. If the patient has chronic diarrhea then the stenosis is a normal response to the lack of formed stool passing through the anus. This is typical after colonic Crohn's has been treated by colectomy and ileorectal anastomosis. These strictures are usually less symptomatic and are discovered when the patient has a colonoscopy. If the patient is asymptomatic, they are left alone. No attempts are made to thicken the stool. If the patient is symptomatic, the stricture can be dilated, although splitting the anoderm will cause recurrence of the stenosis.
 - b. If the stricture is Crohn's related due to scarring and sepsis, the Crohn must be treated and the stricture can be dilated. Narrow, web-like strictures can be incised, often with permanent benefit. A stricture related to active sepsis will not resolve until the sepsis is treated.
 - c. Skin-level strictures are often postsurgical. If there is definitely no pCD, or if it is absolutely in remission, then anoplasty may be considered.
 - d. In patients with chronic anorectal Crohn's disease, an anorectal stricture may be malignant. Any hard or resistant stricture should be purposefully biopsied.
- iv. Perianal abscess: If a patient with Crohn's disease develops perianal sepsis, the number one priority of management is to gain control over the sepsis. This is best achieved by an EUA after all the abscesses and fistulous tracks are identified. Prior to the EUA, intravenous antibiotics are usually started, using broad-spectrum agents. Metronidazole and ciprofloxacin seem to have a particularly beneficial effect on perianal Crohn's disease, although metronidazole has side effects that can be difficult for the patients to tolerate.
1. The EUA: There is usually one abscess and one track, but the situation can be considerably more complex than this. An abscess is drained by making a cruciate incision over it, excising the corners and inserting an appropriately sized mushroom catheter. There is no need to break down loculations. A culture of the pus should be obtained. Skin incisions should initially be kept to a minimum, as the presence of pCD means the incisions may never heal. A large subcutaneous cavity in the perineum can be drained with an initial incision and a counter incision made at the opposite ends of the widest diameter of the cavity. The incisions are connected by a Penrose drain of the widest possible diameter that is then tied in a circle (→ Fig. 3). All septic cavities are drained with a mushroom drain. The anus can be inspected and searched to find the guilty crypt. This can then be drained with a vessel loop seton if it is obvious. Probing for an internal opening at the initial EUA and drainage is not recommended, as it is easy to create false tracks and internal openings.
 2. Postoperatively, frequent assessments are made of the progress of the sepsis. If the first examination under anesthesia does not control the sepsis (decreasing pain, swelling, and cellulitis), another is scheduled.

Fig. 3 Drainage of a large perianal abscess in a patient with Crohn's disease: use of counter incisions with Penrose drains to gain control of the sepsis. There are two vessel-loop setons and one mushroom catheter draining a cavity.

This is to make sure that no abscesses/cavities/tracks have been missed. If the patient still has signs of systemic toxicity, or if the bowel movements are interfering with sepsis control, a diverting stoma is performed. The patient should be consented appropriately before the procedure. Once the sepsis is settled, tube drains and setons can be downsized or removed. Continued drainage implies the presence of a fistula and an elective EUA allows judicious probing to identify likely internal openings. If a stoma is made to divert stool from otherwise uncontrollable perianal sepsis, the odds of closing that diversion are low.⁵

3. Fistula: Anal fistulas in patients with Crohn's disease are challenging. This is reflected in the literature where multiple different ways of managing them are described. Here is a way of approaching the challenge.
 - i. Identify the correct internal and external opening (s). Every anal fistula has at least one internal and one external opening. In cryptoglandular fistulas, these are almost always single, and the internal openings are either directly anterior or posterior. Crohn's-related fistulas can have multiple internal and external openings, and the internal opening(s) can be eccentric. The external openings are generally obvious. The internal opening may be difficult to connect with the external, as fistula tracks can be tortuous and exist in multiple planes. Gentle and sensitive probing is the best way of finding the correct track. The aim of the initial assessment is to find the fistulas and control the sepsis (see above). Probing may be augmented by injection of the track with saline, hydrogen peroxide (do not use when there is a cavity associated with the track), or methylene blue.
 - ii. Many authors recommend imaging of the anus to help define the sepsis. Magnetic resonance imaging, computed tomographic scanning, or simple fistulography have all been described and may

have a place. In general, we have found that a careful, sensitive EUA is the most accurate way of defining disease, and has the advantage of allowing drainage as well.

- iii. The other aim of the initial assessment is to diagnose pCD. If it is present, then surgery must be delayed until the disease is in remission. This will mean initial therapy with biologic agents, once the fistula is drained by a seton and the perianal sepsis is controlled.
- iv. Once the sepsis is controlled, the fistula track is drained, and perineal Crohn's is treated (or not present), definitive fistula repair may be considered. This is approached in different ways according to the depth and complexity of the fistula(s). The principle is that the fistula is kept active through the entry of bacteria into the track at the internal opening. Healing the fistula requires that the internal opening is successfully treated. The same procedures that apply to anal fistulas in patients with cryptoglandular sepsis apply in those with Crohn's-related fistulas. Fistulas in the setting of pCD are different in that the Crohn's itself is part of the fistula and needed to be treated as well as the track. Here is where preoperative optimization with biologic therapy is important.

Fistulotomy is an option in subcutaneous fistulas or very superficial transsphincteric fistulas (not anterior in women). In the transsphincteric fistulas, a cutting seton can be used. Fistulotomy can be a disaster in patients with perineal Crohn's (►Fig. 1) and must not be performed if this is a possibility. It is better to leave a seton in long term than create a perianal wound that will never heal.

Advancement flap repair is a good option in transsphincteric or suprasphincteric fistulas. Here the track has to be effectively drained so that it is not inflamed but rather uncomplicated (no cavities) and fibrotic. This needs seton drainage for at least 6 weeks. Second, the anoderm has to be intact. It is impossible to repair the internal opening when the anoderm or low rectum is ulcerated. In patients with pCD, this usually needs treatment with biologic agents so that the epithelium is healed before surgery is attempted. The benefits of this approach are shown in ►Table 1. If the anoderm cannot be healed then long-term seton drainage can improve symptoms and make the situation tolerable. Jarrar and Church described this technique of the advancement flap and results in Crohn's-related fistulas.⁶ In 33 patients with Crohn's disease and anal fistulas, the success rate of advancement flaps in achieving complete healing was 87%.

Complex perianal Crohn's disease with multiple interconnecting fistula tracts can sometimes be managed definitively by a sleeve excision of the low rectum and dentate line. This is a complex surgery that requires fecal diversion and possibly a Turnbull–Cutait approach to

anastomosis, and should not be attempted by inexperienced surgeons.

Ano and recto vaginal fistulas present a particular problem in patients with Crohn's disease. They are usually more symptomatic than perianal fistulas, although the symptoms are less often due to sepsis than to incontinence of stool. The leaking stool causes intense and painful local irritation. Insertion of a seton will not help unless the fistulas are septic (which is unusual); septic fistulas are usually to the labia rather than truly into the vagina. There is a higher rate of diverting stomas in patients with fistulas to the vagina. Repair is a challenge because fistulotomy is not advisable for fear of permanent incontinence, and the relative lack of muscle in the anterior perineum makes effective advancement flap repair less successful. If the perineum is thin, sphincter repair may succeed in repairing the fistula and improving continence. Treatment of perineal Crohn's is essential for success in healing the fistula, and failure is a potential reason for an abdominoperineal excision of the rectum and anus.

4. Hemorrhoidectomy in the presence of Crohn's disease

There are two issues to discuss within this heading. The first is to establish that hemorrhoids are the cause of the symptoms (usually pain on defecation and bleeding), and the second that management of the hemorrhoidal disease is safe.

Everyone has hemorrhoids; they are normal anorectal structures. Internal hemorrhoids become symptomatic due to prolapse which allows descent into the anus where the passage of stool and the tight anal tone cause bleeding and discomfort. Third- and fourth-degree internal hemorrhoids may also cause mucus leakage from the anus with consequent irritation and pruritus. Third-degree internal hemorrhoids can usually be banded and fourth-degree internal hemorrhoids usually need excision. The frequent stooling and straining that is common in patients with Crohn's disease make patients prone to symptomatic hemorrhoids. Treating the Crohn's disease effectively will usually restore more normal defecation and allow the hemorrhoidal complaints to be treated more conservatively. If symptoms do not improve, the hemorrhoids are treated on their merits, as long as there is no perineal Crohn's. Here, the usual rule applies: treat the perineal Crohn's with biologics and see if the symptoms improve. If the perineal Crohn's settles but the hemorrhoids are very symptomatic, it is reasonable to treat them. If the perineal Crohn's remains active, do not disturb the anorectal epithelium. Cracco and Zinicola recently examined the literature on hemorrhoidal treatment in patients with inflammatory bowel disease.⁷ In 11 retrospective studies with a total of 135 patients, there was a higher rate of complications in Crohn's patients (17%) than those with ulcerative colitis (5.5%).

Literature Review

The most challenging manifestation of perianal Crohn's disease is fistula disease, because of painful associated sepsis, an irritating discharge, and the capacity for spread through abnormal perineal tissues. There are an increasing number of options for the management of anorectal fistulas in patients with Crohn's disease, as novel techniques push the boundaries of therapy. However, none of them refer to the concept of pCD in the effective management of affected patients and so all tend to "miss the boat."

Alternative surgical techniques include fistulotomy, which is a bad idea in any patient with Crohn's disease because the inherent risk of diarrhea makes them especially prone to incontinence, and the Ligation of the intersphincteric tract (LIFT) procedure. While the LIFT is increasingly popular in the treatment of cryptoglandular fistulas, it has had indifferent results for patients with Crohn's disease. Recently, Kamiński et al reported on 23 patients who underwent LIFT, and had a healing rate of 48%.⁸ This was a small series, but the only factor predicting better outcome was the presence of associated small bowel rather than colonic disease. Figg and Church noted that colonic disease is more likely to be associated with pCD and the relatively poor results reported by Kamiński et al may be at least in part explained by the presence of perineal Crohn's.

Endoscopic Therapy

Shen recently described an array of endoscopic procedure for the treatment of perianal fistulas in patients with Crohn's disease.⁹ These include endoscopy-guided seton insertion, endoscopic fistulotomy, and endoscopic administration of medical agents, plugs, stromal, or stem cells. By definition, these techniques attempt to deal with the complication of Crohn's from the aspect of the rectoanal mucosa, ignoring the perineal skin. While some of these techniques hold promise, they require specialized experience and none have been trialed against more conventional methods of treatment.

In a current review of the topic, Kelley et al summarized the effectiveness of biologic therapy with infliximab and adalimumab, and hyperbaric oxygen therapy,¹⁰ while others used topical tacrolimus.¹¹ Their conclusions were that nothing was as effective as surgery. Stem cells are a recent feature of nonsurgical therapy, but in the presence of active pCD nothing but biologic therapy is likely to be effective. If there is no pCD, then the likelihood of success of these ancillary therapies is higher. De Groof et al performed a meta-analysis comparing seton drainage of fistulas with biologic treatments, finding considerable variation in the results of different studies.¹² Some of the variation in results is likely due to differences in the proportion of patients with and without perineal disease between the studies. Yassin et al did point out the potential benefits of combined biologic therapy and surgery compared with either therapy alone, without apparently appreciating the reason why this might be so.¹³ However, it reinforces the lesson learned so strongly in the data shown in **Table 2**. Local injections of anti-TNF- α antibodies have been attempted, and report some success in improving symptoms.

Summary

While experimental approaches to patients with perianal Crohn's disease showed variable amounts of promise, a common theme in fistula management is that a combination of surgical treatments with anti-TNF α antibody therapy has additional beneficial effects compared with surgery or medical therapy alone. The real explanation for this lies in the differentiation of patients according to the status of their perineum. If there is evidence of Crohn's disease infiltrating the perineum, the use of setons to control the symptoms while biologic therapy treats the disease makes sense. Once the perineum and anoderm is healed, then surgical repair can be attempted. If there is no evidence of pCD, surgical repair can be attempted once the sepsis is controlled. No biological therapy is needed.

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