



## Perianal Crohn's Disease

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### Abstract

Perianal Crohn's disease can be extremely debilitating. Patients may present with a myriad of problems including abscess, simple and complex fistulas, stenosis, ulcers, painless fissures, perianal pain and incontinence. In one-third of patients perianal involvement precedes the onset of symptomatic intestinal disease. The more distal the bowel involvement the greater the prevalence of perianal disease. The majority of patients with rectal Crohn's will have perianal involvement. Control of proximal disease may attenuate the severity of distal disease, however symptomatic perianal disease requires a tailored approach according to patient needs. Atypical perianal

symptoms should raise an index of suspicion for underlying malignancy. Complex Crohn's fistulas are often recurrent and difficult to manage. Infliximab promotes fistula closure prolonging preservation of sphincter function. In the presence of perianal sepsis the principle is early and adequate drainage with definitive management once the sepsis has resolved. Patients should be aware that at present there is no cure and that the purpose of treatment is to keep the patient continent and comfortable. Proctectomy and or a defunctioning stoma may ultimately be indicated in patients with severe perianal disease refractory to medical therapy.

**Keywords:** Crohn's disease, perianal sepsis, fistula, infliximab, carcinoma.

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### Introduction

Perianal disease is often the first manifestation of Crohn's and may precede proximal symptoms by several years (1). Isolated perianal disease persisting in the absence of intestinal disease is infrequent whereas fifty percent of patients with intestinal manifestations of Crohn's will have perianal involvement (2, 3). The prevalence of perianal Crohn's is hard to estimate and in the absence of perianal sepsis, anorectal involvement may be relatively asymptomatic. Perianal pain and faecal or purulent soiling greatly diminish quality of life (4).

It is important that a clinical suspicion of perianal Crohn's is supported by histopathological findings although ulcerative colitis and Crohn's share many common features including cryptitis and crypt abscess (5). Typical features of Crohn's include non-caesating granulomas and transmural ulceration. Granulomas are not found in all cases of Crohn's disease but, when present, suggest higher disease activity (6). A diagnosis of

perianal Crohn's necessitates imaging of the proximal gastrointestinal tract. Small bowel follow through and colonoscopy will help to determine the presence of proximal disease and level of activity. Some centres favour MR enteroclysis quoting superior quality in detecting small-bowel pathology and mucosal irregularities in addition to improved patient compliance and reduced radiation exposure (7, 8).

There are a number of questionnaires that are used to determine patient's quality of life with Crohn's disease. Perianal disease activity scores are particularly used in clinical trials to assess response to treatments. The Perianal Activity disease Index (PADI) gives an effective evaluation of the perianal morbidity caused by Crohn's disease. This index concentrates on five areas: discharge, pain, restriction of sexual activity, type of perianal disease and degree of induration (9). Epidemiological, clinical, and molecular studies have provided strong evidence for a genetic



contribution to the pathogenesis of Crohn's disease (10, 11). Recent molecular data suggests that genetic factors may underlie the disease heterogeneity observed in perianal Crohn's disease. Work by Armuzzi et al. identified that the IBD5 risk haplotype is associated with Crohn's disease only and genotype-phenotype analysis

reveals that the strongest association is observed in patients with perianal Crohn's disease. IBD5 risk haplotype H2 spans 250 kb, encompassing a number of immunoregulatory genes suggesting that perianal disease may result from dysregulated immune responses to site specific bacterial colonisation (12).

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## Presentation

Many patients present with minor perianal problems including skin tags, painless fissures, superficial fistulas or haemorrhoids. More often than not conservative management is appropriate (13). Treatment decisions should be guided by patient symptoms and not by the appearance of the perineum that may be quite distorted despite the patient been asymptomatic. The dangers of over enthusiastic local surgery for minor disease are incontinence and fistula formation. In patients with Crohn's disease who have skin tags and haemorrhoids, conservative management is advised because of the post-operative risk of poor wound healing, anorectal stenosis and the potential need for subsequent proctectomy (14). This includes banding of haemorrhoids. Anal fissures in patients with Crohn's disease tend to be painless and are not associated with an increase in resting anal sphincter pressure. 80 % heal with conservative management. Before considering a lateral internal sphincterotomy or endoanal flap one must ensure that the perianal pain is due to the fissure and not co-existing sepsis.

The most common presentation is perianal sepsis. Very often this is associated with a fistula that

should be managed only after the underlying sepsis has resolved. Most anorectal infections begin in the cryptoglandular area at the level of the dentate line, giving rise to an abscess that may track in a variety of directions. It may also result from an obstructed fistula tract. The presence of severe perianal pain in the absence of clinical findings should raise an index of suspicion for an ischiorectal, intersphincteric or supralelevator abscess. An ischiorectal abscess often points to an area a few centimetres lateral to the anal verge and is generally associated with a transsphincteric fistula. The early diagnosis of perianal sepsis in all patients including those with Crohn's disease is critical as ongoing unrecognised infection may lead to necrotising fasciitis. This is a particular risk for Crohn's patients who are immunosuppressed.

The key to emergency surgery is to adequately drain the abscess while avoiding anal sphincter damage (15). If there is a large associated ischiorectal cavity then a catheter, such as a Malecot, may be left in-situ to facilitate drainage. Once the underlying sepsis has resolved the patient may undergo an elective EUA followed by definitive surgical or medical treatment.

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## Radiological imaging of perianal Crohn's disease

Radiological imaging plays a central role in the assessment of patients with Crohn's disease. It helps in determining the level of disease activity and associated complications (7, 16).

The role of MRI in evaluating the anorectal complications of Crohn's disease is well defined. Most radiologists perform external coil MRI avoiding the use of endoanal coils, primarily due to patient discomfort. Accurate assessment of perineal disease is based on a comprehensive knowledge of anal sphincter anatomy and signal characteristics at imaging (17). MRI is particularly useful in the identification of undiagnosed fistula tracts and is also used in monitoring the effects of medical treatments. Van Assche et al. reported that despite apparent fistula healing after infliximab therapy, some fistula tracks persist with varying degrees of residual inflammation (18).

Endoanal ultrasound is an important adjunct in assessing perianal disease. It is limited in patients with perianal pain and anorectal stenosis. It is accurate in identifying anal sphincter defects and the internal opening of an anal fistula (19). Fistulography and pelvic CT are not sensitive enough in delineating perianal disease and have become redundant (4).

Schartz et al. showed that endoscopic ultrasound, magnetic resonance imaging and examination under anaesthesia have a high predictive potential for classifying perianal Crohn's disease. They propose that a combination of either pelvic MRI or rectal EUS and surgical evaluation may be the optimal approach and that the exact imaging modality used depends on the local expertise available (20).

## Surgery for perianal Crohn's disease

Low anal fistulas are best treated by laying open the fistula tract in a one or two stage procedure. A curved probe is used to identify the fistulous tract with care taken to avoid iatrogenic injury. The skin, fat and distal anal sphincter, are divided over the probe and the tract curetted. Anterior fistulas are usually radial whereas posterior fistulas may be curved and have multiple external openings from a single internal midline opening. In the absence of rectal involvement healing rates are high (21, 22).

A draining seton is the treatment of choice in patients who have active perianal sepsis, proctocolitis or in patients with complex perianal fistulas (23). Setons are quite tolerable and provide a bridge to medical therapy. Patients may have several tracts that give rise to multiple openings, often referred to as the "watering- can perineum" (24). Hydrogen peroxide or methylene blue may help in identifying the internal opening (25, 26). Once the sepsis is controlled, infliximab will promote fistula closure. A draining seton is usually removed after the second dose of infliximab. In complex perianal fistulas, several draining setons may be placed at one time. Once the fistula tracts have closed, maintenance therapy with azathioprine, 6-mercaptopurine or infliximab may be used, however no long-term comparative data are available. If a combination of these treatments fail, the patient may ultimately require proctectomy.

There are several medical options available as an adjunct to surgery in the management of fistulizing Crohn's disease (27, 28). Antibiotics such as metronidazole and ciprofloxacin have been used on the basis that bacterial flora, especially anaerobic organisms, contribute to perianal sepsis, however the disease tends to recur once the antibiotics are discontinued (29, 30). Cyclosporin results in approximately an 80% response rate and works by blocking the T-helper and cytotoxic lymphocytes. Unfortunately the benefits are most often temporary and drug toxicity may result in hypertension, renal failure and secondary infections (31). Thus cyclosporin is often used as a bridge in severe disease while awaiting onset of slower acting medications such as azathioprine (AZT) (32).

Infliximab is a genetically engineered monoclonal antibody that blocks interaction of TNF- $\alpha$  and may cause lysis of TNF- $\alpha$  producing cells (33). Two randomised trials have shown that a 3- dose regime administered at 5 mg/ kg is effective in promoting the closure of fistulas (34, 35). One of the limitations of all drugs is the high recurrence rate once the medication is discontinued or levels fall below a certain therapeutic window.

Fibrin glue has been successfully used in the treatment of anal fistulas. The injection kit consists of fibrinogen and thrombin. The success rate is quoted at 60% rising to 70% following re-treatment (36). It is associated with minimal complications, no functional impairment and again avoids sphincter damage (37). It may also be used in complex anal fistula and if unsuccessful has no detrimental effect on subsequent therapies (38, 39).

Endorectal advancement flap is an alternative to fistulotomy or draining setons in patients with rectal sparing (40). The internal and external openings of the fistula tract are identified and the tract curetted. Underlying tissues are infiltrated with a dilute adrenaline solution to minimize bleeding. The flap is broad based and rhomboid shaped consisting of mucosa, submucosa, and internal sphincter. The initial incision is made approximately 0.5 cm distal to the internal opening, parallel to the dentate line and advanced in a cephalad direction. It is usually 4 to 5 cm in length allowing the apex to be trimmed so that the internal opening of the fistulous tract is excised and subsequently covered by fresh tissue. An alternative is to use a perianal skin flap advancement into the anal canal. The major advantage of these flaps is minimal trauma to the external anal sphincter (41, 42). Modifications of this include the rectal sleeve advancement flap as initially described by Berman (43). Other alternatives include dermal-island flaps or cutaneous advancement flaps such as a Martius flap that utilizes a fat pad of the labium majora with the underlying bulbocavernosus muscle, mobilized on a posterior pedicle containing the perineal branch of the pudendal artery (44). A flap may also be obtained from the perineal groin crease.

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## Faecal diversion

The beneficial effects of faecal diversion in Crohn's disease were first reported by Truelove (45). Approximately 50% of patients with symptomatic perianal Crohn's will require permanent faecal diversion (46). The traditional indication for faecal diversion alone in Crohn's

disease was severe perianal sepsis, deep persistent anal ulceration, complex anorectal or rectovaginal fistula in addition to complications refractory to medical and local surgical measures (47).



There is an initial high rate of perianal healing with restoration of bowel continuity possible in those with rectal sparing. However in patients with rectal or colonic Crohn's involvement, restoration of bowel continuity almost invariably leads to

recurrence of perianal symptoms eventually necessitating proctectomy. The key is to identify those patients who will benefit from temporary faecal diversion in whom restoration of intestinal continuity will be possible at a later stage.

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## Proctectomy

Proctectomy may be required when medical and surgical therapy fails to control perianal disease and its complications. It may also be indicated when the side effects of medications are intolerable. Proctectomy is more common in patients with active rectal Crohn's disease and who have had multiple previous surgeries for anorectal disease.

Patients may have colonic involvement that necessitates proctocolectomy with permanent end ileostomy. In ill or high-risk patients this may be performed in two stages with an initial colectomy and end ileostomy followed by completion proctectomy. In contrast to an abdominoperineal resection for rectal cancer, an intersphincteric dissection may be considered for the perineal

component, however deep fistulating disease or sepsis may make this impossible (48).

One of the well-recognized complications of proctectomy is a persistent perineal sinus. Where a tension free closure is not possible the use of rectus abdominus, gluteal myocutaneous and gracilis transposition flaps promote healing (49). If a sinus persists it is important to outrule pelvic sepsis or an enteroperineal fistula that would necessitate resection of the affected bowel.

Some patients post proctectomy will have phantom sensations analogous to that following limb amputation (50). Explanation and reassurance is usually sufficient. Persistent perineal pain post proctectomy can be troublesome and may be caused by a neuroma.

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## Special considerations

### *Rectovaginal fistula*

Rectovaginal or anovaginal fistulas occur in 3 % to 10 % of Crohn's patients. Symptoms include passage of faeces, pus, gas and a foul smelling discharge per vagina. The persistent faecal discharge leads to excoriation of vaginal mucosa. Low anovaginal fistulas may discharge intermittently and are difficult to diagnose. In contrast large rectovaginal fistulae giving rise to faecal soiling and pelvic sepsis are easy to identify. Investigations include proctoscopy, vaginal examination, barium enema and vaginography. EUA will also help in identifying the anatomical location of the fistula. A draining seton may be required for control of sepsis. In the presence of severe pelvic sepsis the patient may

require a defunctioning stoma. Medical treatments used to promote fistula closure include 6-Mercaptopurine, cyclosporine, tacrolimus and infliximab. If the fistula persists after medical therapy and there is no evidence of an anorectal stricture or active rectal disease, then surgical repair should be considered.

For low fistulas with quiescent rectal disease, a mucosal advancement flap or local flap may be suitable. A transvaginal approach with a diverting intestinal stoma may also be used (51). High rectovaginal or colovaginal fistula may be best approached from the abdomen (52). Some women may choose to accept residual fistula drainage over proctectomy or stoma formation.

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## Rectal stenosis

Rectal and anal strictures may cause obstructive symptoms. Patients will generally have underlying proctitis and severe perianal disease (53). The stricture may be primary or occur as a complication of anorectal or ileal pouch surgery performed on a preoperative presumed diagnosis of ulcerative colitis. Dilation may be performed with Hegar dilators or an endoscopic balloon (54).

Perforation is a risk but this represents a viable alternative to surgery particularly in high-risk patients and in younger patients in whom operative intervention would further reduce fertility potential (55). Severe symptoms which do not respond to dilation may require an advancement flap. Anorectal stenosis may ultimately require faecal diversion or proctectomy (56).

## Association with carcinoma

There is an increased risk of gastrointestinal carcinoma in patients with Crohn's disease (57, 58). Risk factors for anal or rectal cancer include severe complicated disease involving the rectum and perianal region with an early onset and prolonged duration (59, 60).

If there is an index of suspicion then EUA with biopsies and curettage of fistulous tracts will increase the diagnostic yield (61, 62).

The histopathology reported has included squamous and adenocarcinoma. Adenocarcinoma

arising in long standing perianal Crohn's disease mandates proctectomy. Squamous carcinoma may be considered for chemo-radiotherapy however the functional outcome may be unsatisfactory. In this situation proctectomy may be the preferred option.

Thus when managing Crohn's patients with perianal disease one should be aware of their increased potential for carcinoma. Any change in perianal symptoms should raise an index of suspicion for malignancy.

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## Perianal disease and pregnancy

Crohn's disease shows a peak incidence in females during their reproductive years (63). Thus a percentage will have active or new onset perianal disease during pregnancy. Patients with inflammatory bowel disease undergo caesarean section more often than that of age, matched

controls (64). Beniada et al. found that for those with inactive or absent perianal disease, vaginal delivery did not significantly exacerbate or trigger disease relapse. Thus, while active disease may be an indication for caesarean section, it is not required for those with quiescent disease (65).

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## Conclusion

As with all aspects of Crohn's disease a multidisciplinary approach that involves surgeons, gastroenterologists, dieticians, nurse specialists and radiologists is central to a successful outcome. Education is of critical importance, as

patients must understand that while surgery will improve quality of life it does not provide a cure. The ultimate aim of management is the eradication of perianal sepsis and to keep the patient continent and comfortable.

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