



# Journal of Coloproctology

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## Letter to the Editor

# Fistulizing perianal Crohn's disease – update and new ongoing treatments



Dear Editor,

Perianal involvement is one of the most important manifestations of Crohn's disease (CD), and it affects up to 30–40% of these patients. Usually, CD affects young patients and it is associated to high morbidity and negative impact in the quality of life. The clinical treatment has been improved in the last decade with the large use of immunosuppressant drugs and the advent of monoclonal antibodies, such as the anti-TNF- $\alpha$  (anti-tumor necrosis factor alfa). The best results in the treatment of perianal CD depend on the appropriate drug management and surgical approach.<sup>1</sup> The boundaries between medical treatment, which involves the management of increasingly specific drugs, and surgery are not easy to establish. The association of both is better than isolated therapies, mainly for complex fistulizing perianal CD. This is due to the fact that CD is a chronic, recurrent disease whose etiology is not fully elucidated. For this reason, surgical indications are restricted to the treatment of the disease's complications and its clinical intractability.

About 70–80% of patients will undergo a surgical procedure during their follow-up, and perianal surgical procedures are part of those surgeries. The surgery does not promote the cure of the disease and therefore the decision to operate can be difficult and depends on the surgeon's experience in handling this type of condition. Best clinical management has influenced the timing of surgical indication, delaying or even avoiding it. However, it is still a conflicting issue and more prospective studies are required. Relapse of CD after surgery may occur in patients considered to be high risk, such as being young at the onset of the disease, smoking habits, family history of CD, and fistulizing phenotype. In this sense, the decision for surgery depends on the aggressiveness of the perianal CD and the concomitant involvement of the colon and/or small intestine. Furthermore, it is important to establish CD phenotypes, which can be inflammatory, stenotic and/or fistulizing. The fistulizing form of the disease is related to higher incidence of recurrence and indicates its progression.

Indication for surgery, concerning perianal CD, includes the presence of abscesses and fistulas that remain active even with the use of immunosuppressant and/or biological therapy.

Preoperative imaging studies, such as magnetic resonance imaging (MRI) of the anal canal and/or endoanal ultrasonography, can help identify abscesses which are sometimes smaller and deeper, but symptomatic. They can also delimit the location of the abscesses in relation to the anal sphincters and the involved portion of the anal canal.<sup>2</sup> Additionally, these exams allow the identification of the course of perianal fistulas, showing the degree of involvement of the sphincter muscles. Endoanal ultrasonography is limited in cases of severe stenosis of the anal canal, which makes it impossible to introduce the device.

Perineal examination under anesthesia and surgical procedures should consist of draining abscesses and exploration of fistulas by placing seton, which can remain for a long period. Fistulotomy without repairs should be restricted to very shallow paths that do not compromise the sphincter muscles. Another option to consider is the endorectal advancement flap, which has been used in the treatment of complex or recurrent fistulas, and healing is observed in 60–70% of CD patients.<sup>3</sup>

The use of fibrin glue in the treatment of CD perianal fistula showed efficacy in the treatment of complex fistulas, but no advantages in the case of simple fistulas when compared to conventional treatment.<sup>4</sup> Fibrin glue seems to be less effective in patients with CD, but is well tolerated and has a minimal risk profile, and could be used to avoid further surgery or as an alternative to long-term seton placement. The fistula plug is another treatment option that has been studied for perianal fistula. It is a portion of lyophilized porcine intestinal submucosa and acts as a collagen scaffold, which is filled by endogenous cells. Reported healing rates were 54.3% in CD patients at follow-up between 3 and 24 months, which did not differ from patients without CD. The extrusion of the plug is the main reason for secondary failure of this technique.<sup>5</sup>

Mesenchymal stem cell (MSC) therapy for CD represents a promising strategy and has been studied for luminal disease.<sup>6</sup> To assess the efficacy of MSCs for CD-related fistulas, the ADMIRE-Crohn's disease multicentre study is underway (<http://www.clinicaltrials.gov/ct2/show/NCT01541579>). This protocol evaluates the use of adipose derived mesenchymal stem cells (administered by intralesional injection) for

induction of remission in perianal fistulizing CD, and the estimated primary completion date is the beginning of the next year with promising results. The main advantage of this technique is the sphincter preservation, avoiding repairs or fistulotomy.

Not infrequently, perianal fistulas are accompanied by extensive CD involvement of the rectum, which can lead to loss of the rectum and anal canal, exhausting even the best in clinical therapy, requiring proctectomy and permanent ostomy.

In summary, perianal CD is a common manifestation of the disease and if it is concomitant to rectal lesions, the clinical and surgical management may become complex. Despite all developed drugs and new surgical techniques, there is a failure rate that is not negligible. Some cell therapies, such as MSCs, and new drugs that act upon other specific immune targets may be promising treatments for complex and/or recurrent fistulizing CD in the future.

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### Conflicts of interest

The authors declare no conflicts of interest.

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