

Injection of Freshly Collected Adipose Tissue for the Treatment Complex Cryptoglandular Anal Fistula: Case Report

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Abstract

Introduction Perianal fistula is a common colorectal disease which is caused mainly by cryptoglandular disease. Although most cases are treated successfully by surgery, management of complex perianal fistulas (CPAF) remains a challenge with limited results in recurrence and sometimes associated with fecal incontinence. The CPAF treatment with autologous adipose-derived mesenchymal stem cells (ASCs) had become a research hotspot. The technique started to be used in the treatment of Crohn's disease (CD) fistulas, where the studies showed safe and good results from the procedure. Cultured ASCs have been used but this approach requires the preceding collection of adipose tissue, time for isolation of ASCs and subsequent in vitro expansion, need for laboratory facilities, and expertise in cell culturing. These factors have been getting over by using the commercially available alternative, allogenic ASCs. Treatment with allogeneic ASCs has shown good results in patients with CD fistulas, however with the disadvantage of being expensive. **Objective** To show that the injection with freshly collected adipose tissue is an alternative to treatment with autologous or allogenic ASCs with several advantages. **Methods:** In this case report, we show our first experience in the treatment of CPAF with the application of collected adipose tissue in a tertiary referral hospital from Belo Horizonte, Brazil. **Results** The patient had a good postoperative recuperation with a complete fistula healing after 8 months without adverse effects. **Conclusion** Injection with freshly collected adipose tissue is a promising and apparently safe sphincter-sparing technique in the treatment of CPAF.

Keywords

- ▶ cryptoglandular
- ▶ Fistula-in-ano
- ▶ perianal fistula
- ▶ freshly collected adipose tissue
- ▶ adipose-derived stem cell
- ▶ stem cell therapy

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Introduction

Perianal fistula is a common colorectal disease with an incidence rate of 1.1 to 2.2 per 10,000 population per year, which is caused mainly by cryptoglandular disease.^{1,2} Although most cases are treated successfully by surgery, management of complex perianal fistulas (CPAF) remains a challenge with limited results in recurrence and sometimes associated with fecal incontinence.³⁻⁵ Several sphincter-sparing surgeries are emerging, including minimally invasive surgery, but the most suitable surgical treatment has not been determined.

The application of autologous adipose-derived mesenchymal stem cells (ASCs) emerged as a novel approach for enhancing the regeneration and repair of damaged tissues in an environment particularly unfavorable for wound healing. Previously ASCs have been used as a treatment for diabetic foot, inflammatory bowel disease, and osteoarthritis, because of their many advantages compared with other sources of stem cells.^{6,7} Treatment of CPAF with the application of ASCs is a sphincter-sparing technique that has been reported as a safe and effective technique.⁸

The treatment of CPAF with application of ASCs has become a research hotspot. The technique started to be used in the treatment of Crohn's disease (CD) fistulas, where the studies showed safe and good results from the procedure.⁹ Cultured ASCs have been used but this approach requires the preceding collection of adipose tissue, time for isolation of ASCs and subsequent *in vitro* expansion, need for laboratory facilities, and expertise in cell culturing. These factors have been overcome by using the commercially available alternative, allogenic ASCs. Treatment with allogeneic ASCs has shown good results in patients with CD fistulas, however with the disadvantage of being expensive.¹⁰

The injection with freshly collected adipose tissue is an alternative to treatment with autologous or allogenic ASCs with several advantages. This is a procedure that is readily available and requires minimal preparation, making it accessible to most patients. The treatment is inexpensive and requires a single surgical procedure and there is no need for a laboratory and cell culture as with the use of cultured ASCs.¹¹

In this case report, we show our first experience in the treatment of CPAF with the application of collected adipose tissue in a tertiary referral hospital from Belo Horizonte, Brazil. The patient had a good postoperative recovery with a complete fistula healing after 8 months without adverse effects.

Case Report

A 39-year-old female with the history of renal transplant. She was sent to our hospital for perianal pain associated with multiple openings around the anus, with a discharge of fluid and feces. She referred two surgeries previously for abscesses in the last 2 years. Our first approach was placing a seton in the fistulous tract with relief of the symptoms. MRI revealed a trans-sphincteric fistula, at the 6 o'clock position with a collection and fistulous tract up to the external opening at

the 9 o'clock position, thick tissue of the gluteal region on the right side.

Fistulectomy by video assisted fistula anal treatment (VAFT) was performed with good results immediately but one month after she returned to the hospital with a perianal abscess another procedure was performed and placed two setons. She had several returns in the emergency department for purulent discharge through the fistula, treated with antibiotics. After several failed attempts to treat the fistula, injection of freshly collected adipose tissue into CPF fistulas was performed.

Visual examination before the procedure showed 2 external openings in the right gluteal region communicated by a seton and one internal opening at 9 o'clock communicated by a seton with one of the external openings. Besides patient presented fibrotic tissue in the right gluteal region (→ Fig. 1).

In June 2022 the patient underwent the procedure in the operating room. General anesthesia and antibiotic prophylaxis with ceftriaxone and metronidazole was used. The patient was positioned in lithotomy and fistula exploration discovers two tracts, the first from the internal opening at 9 o'clock to the external medial opening and the second one from the medial external opening to the lateral external opening. Setons were removed and tracts were curettage. Liposuction was performed by plastic surgeons in the posterior wall of the left thigh with a 50-ml syringe and a 3-ml cannula obtaining freshly adipose tissue. A total of 150 ml of fat was collected and was decanted for 30 minutes, then the oil and aqueous layers were discarded while the fat layer is kept. The internal opening was closed with 2-0 polydioxanone (→ Fig. 2) and then the fibrotic tissue was resected. Freshly adipose tissue was injected around the fistula tract using a 21 G cannula to fill adjacent tissues and collapse the fistula. Finally, after fibrotic tissue was resected skin borders were partially closed with 2-0 nylon (→ Fig. 3).



Fig. 1 Visual examination before the procedure.



Fig. 2 Freshly collected adipose tissue



Fig. 3 Visual examination after the procedure.

The patient was hospitalized for three days, in the first postoperative day she had visual analogue scale (VAS) 7/10, in the second postoperative day was VAS 5/10 and the third day was discharged with visual analogue scale (VAS) of 1/10. She used 7 days of oral antibiotics (metronidazole and ciprofloxacin). A complaint of mild discomfort, exudate fluid discharge with no feces, and localized edema were reported for the first two weeks and decreased at the third week. Clinical evaluation of fistula healing, fecal incontinence and VAS were assessed at 1, 3, 5, 9, 13, 20, 24 weeks after treatment showing no fecal incontinence, VAS 1/10

and no limitation on dairy activities (→ **Fig. 4**). In the latest assessment 8 months after de operation completely clinical healing was achieved defined by no symptoms of discharge and no visible external and no palpable internal opening by anorectal digital examination. furthermore, she presented VAS 1/10 and no fecal incontinence symptoms and no limitation in dairy activities.

Discussion

The surgical treatment of CPAF is a challenge for colorectal surgeons and the biggest risk is anal incontinence with incidence rate after fistulotomy of CPAF reaching up to 40%.¹² Hence, the principle of surgical treatment of CPAF has become to cure the fistula while decreasing the risk of sphincter injury.³ Currently the sphincter-sparing surgeries are a trend, but the most suitable surgical treatment has not been determined.

The study of perianal treatment with ASCs is a research hotspot, which has a great prospect and potential future application since study published in 2015 by Garcia-Olmo et al. This was a phase I trial involving five patients and using cultured autologous ASCs which showed the feasibility and safety of ASCs transplantation in the treatment of CD fistulas.¹³

Cultured ASCs has been used but this approach requires the preceding collection of adipose tissue, time for isolation of ASCs and subsequent *in vitro* expansion, need for laboratory facilities, and expertise in cell culturing. These factors have been overcome by using the commercially available alternative, allogenic. Treatment with allogenic ASCs has showed good results in patients with CD fistulas, however with the disadvantage of being expensive.¹⁰

Lundby et al. in 2018 reported the first study assessing the effects of injection with freshly collected ASCs as a treatment for fistulas in a cohort of CD patients. The treatment was safe with results of complete clinical fistula healing in 57% of patients, ceased fistula secretion in 14%, and reduced fistula secretion in 5%, resulting in an overall response to treatment in 76% of the patients.¹⁴ In february of 2023 the same group published a study evaluating the treatment efficacy of freshly collected ASCs injection in CPAF.¹¹ Overall, 51% of the 77 included patients achieved the primary outcome of fistula healing, whereas another 12% reported reduced secretion and decreased anal discomfort. Thus, 63% of all treated patients had a positive treatment outcome. The observed overall healing rate of patients from the injection of ASCs is comparable to outcomes after the injection of cultured autologous and allogeneic adipose tissue-derived mesenchymal stem cells. The study showed the injection of freshly collected adipose tissue was well tolerated and approximately half the patients experienced minor side effects. A total of 4% of the patients experienced serious adverse events requiring surgical intervention and prolonged hospital stay because of infectious complications or bleeding. The observed complication rate in these studies is comparable to or lower than complication rates reported in studies using autologous and allogenic stem cells, or microfragmented



Fig. 4 Visual examination for weeks after the procedure.

adipose tissue, which report rates of serious adverse events at 2% to 24%.¹⁵⁻¹⁷

In previous studies evaluating injection of freshly collected adipose tissue, the collected adipose was centrifuged unlike in our case where the adipose tissue was decanted. The decantation technique is easier and less expensive than a centrifugation technique being an accessible alternative to treatment with autologous and allogenic ASCs.

In summary, in this case the use of Injection of freshly collected adipose tissue for the treatment of CPAF was safe and effective.

Conclusion

Injection with freshly collected adipose tissue is a promising and apparently safe sphincter-sparing technique in the treatment of CPAF. This technique could be an accessible alternative to treatment with autologous and allogenic ASCs and prospective studies on the subject are awaited.

Conflict of Interest
None declared.

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