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Autologous Fat Graft with Mechanical Activation for Chronic Ulcers – A Case Report

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ABSTRACT

In recent years, Autologous Fat Grafting (AFG) and related therapies using Adipose-derived stem cells (ADSCs) have garnered increasing attention for their potential in regenerating tissue. However, the available literature exhibits substantial variation, making it difficult to determine whether AFG is superior to conventional wound care or other treatments. Based on our research findings and other evidence presented in the literature, it appears that adult mesenchymal stem cells from the stromal fraction of harvested fat play an active role in certain processes. Autologous fat, when activated by mechanical method, seems to have even more promising results. We present the clinical case of a 78-year-old male who suffered from right leg chronic osteomyelitis resulting in sporadic episodes of recrudescence and a chronic ulcer. As Autologous Fat Grafting (AFG) becomes increasingly recognized as a viable treatment option for cutaneous wounds, we have incorporated a novel approach to the Coleman technique by utilizing an orbital mechanical force of 97 G on adipose tissue for 6-10 minutes to activate the fat. The patient underwent weekly medications with a progressive improvement of his clinical picture. The treatment of ulcers by fat grafting activated is yielding encouraging results and, in our opinion, could become suitable in all types of ulcers as an additional or alternative procedure with low morbidity.

Keywords: *Adipose Tissue, Chronic Ulcers, Gene Activation, Inflammation, Mechanical Activation, Mesenchymal Stem Cells*

Introduction

A 78-year-old male came to our Emergency Room (March 2017) reporting erythema, edema, and pain localized to the right leg associated with a febrile spur. The patient suffered from right leg chronic osteomyelitis resulting in sporadic episodes of recrudescence and a chronic ulcer.

The patient underwent weekly medications for 59 months. To boost wound healing, autologous fat graft injections were recommended as a valuable procedure. In 2022 the patient underwent one fat grafting surgical procedure with wound improvement but without full coverage of bone exposure. After 8 months a new fat grafting procedure was performed with autologous fat processed by Coleman and activated with mechanical method with promising results.

Osteomyelitis is a pyogenic infection and inflammation of the bone, which remains challenging for both patients and physicians (Reinisch *et al*., 2019).

Osteomyelitis usually presents as an acute infection, but it may evolve into a chronic condition. Treatment generally involves evaluation; staging; determination of microbial etiology and susceptibilities; antimicrobial therapy; and, if necessary, debridement, dead-space management, and bone stabilisation (Schmitt, 2017; Carek *et al*., 2001).

The potential of Autologous Fat Grafting (AFG) as a treatment option for cutaneous wounds is gaining recognition, as preclinical studies suggest that AFG can supply a wealth of cytokines and growth factors that facilitate the regeneration and restructuring of soft tissue (Condé-Green *et al*., 2016).

While there is currently no universally established protocol for Autologous Fat Grafting (AFG), several factors associated with lipoaspirate harvest (Zhu *et al*., 2010; Keck *et al*., 2010; Hassan *et al*., 2014; Raposio *et al*., 2017; Raposio *et al*., 2014), processing (Condé-Green *et al*., 2010; Hivernaud *et al*., 2017), and implantation (Coleman, 2001) have been demonstrated to impact both the viability of Adipose-derived stem cells (ADSCs) and the retention of the graft. The most common method of AFG is based on the Coleman technique (Coleman, 2008).

The technique mentioned above, known as Coleman or lipofilling, comprises two surgical procedures conducted with local anesthesia and potential patient sedation. The first step involves the extraction of adipose tissue from the hips or trochanteric region using a blunt cannula measuring 3 mm in diameter. Afterward, the harvested tissue undergoes centrifugation at 3000 rotations per minute for 3 minutes. This process aims to separate a fraction of the aspirated fat from the waste fraction, which is rich

in triglycerides resulting from the breakdown of the adipocyte component (referred to as the liquid fraction). The resulting pellet represents a portion of adipocyte and stromal-vascular tissue enriched with mesenchymal stem cells. We have added to this the activation with the application of an orbital mechanical force for 6–10 min at 97 g to the adipose tissue, lipoaspirated and treated according to Coleman procedures. This mechanical stimulation activates new properties in fat such as the suppression of the cytokines TNF alpha and IL-1 alpha and the overproduction of the cytokine TSG6, with anti-inflammatory activity. In addition, a large increase in the stemness of the activated fat mesenchymal cells is observed. The use of activated adipose tissue leads to a drastic reduction in both in vivo and in vitro production of IL6, IL1alpha, and beta. These properties reveal an anti-inflammatory action proven by the use of specific animal models and as described in detail in our previous study (Carelli *et al*., 2018).

In this clinical case, we propose the encouraging effects of the use of autologous fat activated with mechanical method on wound healing as a relatively easy-to-perform, cost-effective, and well-tolerated procedure.

The patient received detailed information about the procedure, including its benefits, risks, and potential outcomes. Ethical approval was sought and obtained to ensure that the procedure adhered to ethical guidelines and standards. Informed consent was obtained from the patient, indicating their understanding of the procedure, its potential risks, and their agreement to undergo the treatment voluntarily. This process ensures that the patient was fully informed and had the opportunity to make an educated decision about their participation in the procedure.

Description

A 78-year-old male came to our Emergency Room (March 2017) reporting erythema, edema, and pain localized to the right leg associated with a febrile spur. The patient underwent a left leg amputation after a traumatic injury while using a motor hoe, dating back to 1976. The right leg, although severely damaged by the accident, was addressed with conservative treatment. Since the traumatic event, the patient suffered from right leg chronic osteomyelitis resulting in sporadic episodes of recrudescence, the most recent being treated with unspecified antibiotics at another hospital.

In the suspicion of a new event of osteomyelitis, an RMI evaluation of the right leg was carried out, resulting in no evidence of an infectious involvement of the bone tissue neither at the right knee joint nor distal to it. The RMI pointed out cellulitis-related signal alterations localized caudally to the right knee joint, along the lateral side of the leg.

On clinical evaluation of the right leg, two soft tissue defects were found: the first caudally to the knee joint, the latter on the heel. The former was localized in an area of the skin characterized by scarring and tissue atrophy as a consequence of the above-mentioned traumatic injury. Both skin lesions were reported as subjected to cyclical phases of spontaneous improving and worsening even though never reaching a complete healing state.

On the right leg, a 3 cm wide circular lesion was surrounded by edematous and erythematous skin (Fig. 1). The bottom of the ulcer was covered with fibrin and reached the bone plane resulting in bone exposure. A biopsy of the margins of the skin defect was performed for culture testing. C group Streptococcus was identified, and appropriate antibiotic therapy was administered. After medication with chloramphenicol + collagenase ointment, the ulcer was covered with a sterile plaster. Negative pressure wound therapy, which began the following day, was recommended for the treatment of the lesion with a continuous pressure gradient of -50 mmHg.

Figure 1: On the right leg, a 3cm wide circular lesion was surrounded by edematous and erythematous skin. The bottom of the ulcer was covered with fibrin and reached the bone plane resulting in bone exposure.

The patient underwent weekly medications which were brought forward if needed. The right leg lesion's improvement was slow requiring medications for the following years, propped up by hyperbaric oxygen therapy which was administered in March 2019. Starting the same month, the patient underwent photobiomodulation therapy to hasten the slow-paced healing process of the ulcer.

To boost wound healing, autologous fat graft injections were recommended as a valuable procedure. In 2022 the patient underwent two fat grafting surgical procedures, the first dating March 2022, and the latter in November 2022. Both were performed under local anesthesia. The results are shown in Fig. 2. Autologous Adipose tissue was collected from the patient's hips, after infiltration of an anesthetic solution made up of 100 ml of physiological saline, 10 ml of mepivacaine 10ml/dl, and 10 ml of levobupivacaine 5 mg/dl. The harvested tissue was then centrifuged at 3000 rpm for 3 minutes, following

the Coleman technique. After careful curettage of the ulcer's edges and the exposed bone tissue to find a vital and vascularized plane, autologous fat graft injections were performed in the tissues surrounding the ulcer. The skin lesion was covered with paraffin gauze dressings, sterile gauze, and a cohesive bandage. Proper local anesthesia was administered in each step of the procedure. The patient was discharged the same day of the fat graft procedure and clinical examinations were scheduled for the following weeks.

After 8 months a new fat grafting procedure was performed. Not only the harvested fat cells were processed as stated by Coleman but were also activated with mechanical method. Autologous fat was collected from the patient's hips, after infiltration of an anesthetic solution (10 ml mepivacaine 20 mg/ml, 10ml levobupivacaine 7.5 mg/ml). The harvested tissue was then centrifuged at 3000 rpm for 3 minutes, as stated by the Coleman technique. The purified fat cells were activated. Careful curettage of the ulcer's bone bottom was performed, and autologous fat graft injections were performed in the tissues surrounding the ulcer. The skin lesion was then covered with paraffin gauze dressings, sterile gauze, and a cohesive bandage. Proper local anesthesia was administered in each step of the procedure. The patient was discharged the same day. Weekly clinical examinations and medications were scheduled to assess the degree of epithelialization while waiting for the ulcer to be completely resolved. The latest dressing 2 months after the surgical intervention can be seen in the Fig. 3. As depicted in the images, there was a significant transformation from an initially large and exposed bone ulcer prior to autologous fat grafting. Over time, there was a noticeable and gradual process of reepithelialization. Fig. 2 demonstrates some improvement in the lesion, although there was still an area of bone exposure measuring 2 cm x 2cm in diameter. However, after 2 months of activated fat grafting, a visible reduction in ulcer size was observed, with a measured ulcer of 10 mm x 8mm. Additionally, there was extended reepithelialization leading to coverage of the previously exposed bone.

Figure 2: In 2022 the patient underwent two fat grafting surgical procedures, the first dating March 2022, and the latter in November 2022. Both were performed under local anesthesia. The results are shown in this figure.

Figure 3: This is the latest dressing showing increasing bone coverage.

Discussion

Autologous fat grafting (AFG) has been employed as a cosmetic procedure to address concerns such as volume loss or contour irregularities for a significant duration (Condé-Green *et al*., 2016). In the last ten years, there has been an increasing focus on the regenerative capabilities of Autologous Fat Grafting (AFG) and associated therapies involving Adipose-derived stem cells (ADSCs) (Condé-Green *et al*., 2016).

The stromal vascular fraction (SVF) of lipoaspirate samples contains Adipose-derived stem cells (ADSCs) that have been shown to stimulate neoangiogenesis, activate local stem cell niches, and alter immune responses through the release of bioactive molecules (Bertozzi *et al*., 2017; Zhu *et al*., 2010). Additionally, they can enhance the terminal phenotypes of cells involved in wound healing, such as fibroblasts and keratinocytes (Bellini *et al*., 2017). However, there has been no comprehensive evaluation of various Autologous Fat Grafting (AFG) techniques for wound healing, and it remains uncertain whether any specific approach or combination of approaches is superior. Chronic ulcers on the lower limb constitute a particularly challenging situation with a high risk of morbidity for the patient, often associated with recurrent surgical debridement and, eventually, amputations in a compromised vascularized environment (Luck *et al*., 2018).

Autologous Fat Grafting (AFG) has recently emerged as a promising therapeutic approach for treating cutaneous wounds, and preclinical research suggests that it can supply a wealth of cytokines and growth factors that facilitate the regeneration and restructuring of soft tissue (Condé-Green *et al*., 2016). However, there is insufficient evidence to ascertain whether AFG is superior to standard wound care or alternative treatments. Additionally, it is not clear whether a specific type of AFG technique leads to superior wound healing and how this varies depending on the underlying cause of the wound. Because of substantial heterogeneity in the existing literature, it is not possible to establish any superiority of AFG over traditional wound care or treatment options (Malik *et al*., 2020). Lastly, there has been no comparative

assessment of various Autologous Fat Grafting (AFG) techniques for wound healing, leaving it uncertain whether any specific approach or combination of approaches is superior (Luck *et al*., 2018). Our research (Carelli *et al*., 2018; Klinger *et al*., 2008; Klinger *et al*., 2013; Caviggioli *et al*., 2009; Caviggioli *et al*., 2008; Caviggioli *et al*., 2010; Klinger *et al*., 2010; Klinger *et al*., 2011; Caviggioli *et al*., 2012) and other evidence in the literature suggest an active role of adult mesenchymal stem cells from the stromal fraction of harvested fat. Autologous fat, when activated by mechanical method, seems to have even more promising results. In this case report we wanted to include photographs that clearly showed the rapid improvement of the wound after just one session of activated lipofilling. In our Institute, we are working on a single-center prospective study to evaluate the clinical efficacy of autologous fat grafting in the treatment of keloid scars and retracting, painful and radiodystrophic scars.

Future projects will focus on well-designed, blinded, prospective studies on activated autologous fat. Comprehensive reporting of methodological details, and objective outcome measures will be imperative to uphold scientific rigor and enhance the reliability of the findings.

Conclusion

The treatment of ulcers by fat grafting activated is yielding encouraging results and, in our opinion, could become suitable in all types of ulcers as an additional or alternative procedure with low morbidity.

Compliance with Ethical Standards: Conflict of Interest statement: The authors declare that they have no conflicts of interest to disclose.

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