Online Exclusive

Adipose Derived Regenerative Cell Therapy for Treating a Diabetic Wound: A Case Report

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Abstract: Background. Recent studies have reported on the use of adipose derived regenerative cells (ADRC) as a therapeutic method in wound healing. The present study introduces the first application of successful ADRC therapy for a diabetic foot wound. Case Report. A 63-year-old woman with diabetes mellitus complaining of an opened necrotic wound in the plantar aspect of the right foot was admitted by another surgeon for debridement surgery. Despite multiple efforts, a Chopart’s amputation was performed to salvage rest of the foot. In the early postoperative period, a 2 cm x 2 cm circular ulcer at the heel region and a 1 cm x 2 cm unhealed wound at the previous incision site had formed. Due to resistant diabetic ulcers, the patient was introduced to ARDC therapy (informed consent was obtained). The Celusion System™ (Cytori Therapeutics, Inc, San Diego, CA) was used for autologous generation of ARDC cells—1 cc of the ARDC was mixed with 40 cc of fat graft. Afterward, the ARDC-enriched fat graft was introduced to the heel and plantar region to restore the deficient glabrous tissue. The remaining 4 cc of ARDC were equally injected in a radial fashion to the wound edges. Results. In the postoperative follow-up, accelerated wound healing was observed and the ulcers were completely healed after 4 weeks of ARDC treatment. Conclusion. ARDC therapy has the potential to be a promising new therapeutic modality for treating diabetic wounds.

Introduction

Regenerative medicine points to the utilization of the body’s cells in the healing process. This fact has been introduced to a wide range of applications in which reconstructive surgery occupies an important space. Indeed cells, unlike many matrix molecules and proteins, cannot be manufactured per se. They must be harvested and replicated before clinical use. Moreover, this process must be performed in a manner such that the therapeutic potential of the cells is not dissipated.

The therapeutic potential of using regenerative cells is tremendous. These cells have now been isolated in various tissues, and adipose tissue could be one of the most suitable and abundant cell sources for regenerative therapy.

Recently, studies have shown the potential use of adipose derived regenerative cells (ADRC) as a therapeutic method in wound healing. In this article we introduce the first application of a successful ADRC therapy for a diabetic foot wound.

Case Report

Another surgeon admitted a 63-year-old woman with diabetes mellitus for debridement surgery who had been complaining of an opened necrotic wound in the plantar aspect of her right foot. The patient was followed up for 45 days with the last 2 weeks for negative
pressure wound therapy (V.A.C® Therapy, KCI, San Antonio, TX). Despite all attempts at treatment, the patient was still suffering from a high amount of yellow secretion, especially from the heel region. Culture swabs were obtained and all results were negative. A process of removing fat necrosis was continued and glabrous tissue in the heel region disappeared. The patient was then admitted to the authors' plastic surgery clinic, and after a thorough laboratory make-up, a Chopart’s type amputation was performed to salvage rest of the foot. In the early postoperative period the discharge continued and a 2 cm x 2 cm circular ulcer at the heel region and 1 cm x 2 cm unhealed wound in the previous incision site had formed (Figure 1). Afterward, the patient was followed up for 60 days postoperatively and treated with hyperbaric oxygen therapy for 30 sessions with no apparent changes in wound healing. The patient was started on ARDC therapy and an informed consent was obtained. The Celusion System™ (Cytori Therapeutics, Inc, San Diego, CA) was used for autologous generation of ARDC cells. Under spinal anesthesia, a 500 cc tumescent solution was injected and 400 cc of lipoaspirate was harvested from the abdominal region. 360 cc of the aspirate was introduced to a disposable canister attached to the side of the device to which the collecting and draining tubes are attached. Afterward, the device rinses the tissue with 36˚C heated ringer-lactate solution to purify the tissue. 5.1 mL of Celase™ (collagenase enzyme) was introduced to separate the fat cells from the regenerative cells.

The generated suspension was transferred through an optical sensor to a closed centrifuge system within the device to aggregate the cells. Finally, a 10 x 10^7 regenerative cell (5 cc volume) was collected using a syringe from the centrifuge chambers of the device. Then, 1 cc of the ARDC was mixed with 40 cc of the fat graft. Using a 1 mm lipo-injection cannula, the ARDC enriched fat graft was introduced to the heel and plantar region to restore the deficient glabrous tissue. The remaining 4 cc ARDC were equally injected using a 1 cc insulin syringe in a radial fashion to the free wound edges (Figure 2). In the postoperative follow-up, promising wound healing was observed (Figure 3), and the wounds were totally healed after 4 weeks of treatment (Figure 4).

Discussion
Since Zuk et al1 reported that adipose tissue contains regenerative cells, great attention has been paid by the research community to using regenerative cells in clinical applications. This is because adipose tissue has several advantages over bone marrow as a source of regenerative cells. The abundance of regenerative cells is one such advantage, based on several studies and colonogenic assays, the average number of ARDC in adipose tissue is in the range of 1%, which is about 100-fold that of bone marrow. Other advantages might be the ease of harvest and lower donor site morbidity.

Preliminary studies of the characteristics of autologous ARDCs are similar to those of other human sources for stem cells, and thus, experimental data are applicable to ARDC in regenerative wound healing. Notable potential effects of ARDC include multilineage differentiation mechanisms, paracrine and autocrine signals promote the complex wound healing in regards to epithelialization, angiogenesis, proliferation, and matrix deposition by the fibroblast by means of the aforementioned mechanisms. Adipose-derived...
Regenerative cells have been shown to enhance wound healing through increased angiogenesis, reepithelialization, and granulation tissue formation.\(^5\)

Akita et al.\(^6\) reported the successful use of ARDC therapy with the Celusion system in patients with resistant radiation wounds. More recent studies regarding long-term fat graft retention in breast reconstruction have shown promising clinical results.\(^7,8\)

Recent studies in diabetic animal models have shown the significant positive impact of local stromal stem cell delivery on the wound healing process,\(^9,10\) which have provided a promising path for future clinical trials.

In this case report, the application of ARDC therapy in diabetic wound treatment is presented as the first clinical case in the English literature. In the follow-up period, wound healing was promising. The use of ARDC enriched fat graft for reconstruction of glabrous tissue in both the heel and plantar region presented an innovative method for such a challenging surgery. Moreover, the ease of harvesting and application of the ARDC makes it a favorable modality compared to other regenerative cell resources.

Conclusion

When considering the difficulties in treating diabetic wounds, the results are indeed promising. Moreover, with attention to prospective, randomized, double blind trials, this may be a promising new horizon for diabetic wound treatment modalities.

References


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