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ORIGINAL ARTICLE

Fat Injection for Cases of Severe Burn Outcomes: A New Perspective of Scar Remodeling and Reduction

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Abstract
Background Despite civilization and progress, burns occur frequently in the world. Remarkable discoveries of wound healing mechanisms have been reported. On the other hand, long-term outcomes from burn injuries represent a barrier to improvement of patients' social, functional, and psychological condition. Lipofilling, described since the 1980s, currently is used for several clinical applications. This study aimed to verify whether lipofilling could ameliorate scar remodeling in three clinical cases.
Methods Three adult patients with hemifacial hypertrophic scars and keloids resulting from severe burns 2 to 13 years previously were selected. The patients were treated by injection of adipose tissue harvested from abdominal subcutaneous fat and processed according to Coleman's technique. Two injections (with a 13-month interval between) were administered at the dermohypodermal junction. Histologic examination of scar tissue punch biopsies (hematoxylin-eosin staining) before and after the treatment was performed as well as magnetic resonance scan with contrast.
Results The clinical appearance and subjective patient feelings after a 6-month follow-up period suggest considerable improvement in the mimic features, skin texture, and thickness. Histologic examination shows patterns of new collagen deposition, local hypervascularity, and dermal hyperplasia in the context of new tissue, with high correspondence to the original.
Conclusions The preliminary results show that lipofilling improves scar quality and suggest a tissue regeneration enhancing process.

Keywords Adipose cell · Burn · Liposuction · Scar · Stem cell

During the past 20 years, advances in acute burn therapy [25], including cases with involvement of wide surfaces, have been considerable, allowing survival rates to increase significantly thanks to shock, metabolic alteration, and infection management as well as the use of biotechnologies. Despite this, we cannot find the same improvement in long-term burn outcomes, which still are a social, economical, and psychological problem in terms of both functional and aesthetic aspects.

The current mainstay treatment for long-term burn outcomes is limited to surgery, physiotherapy [5], laser [1], steroid [3], and silicon film [4] application. The use of radiotherapy [20] or drugs, such as colchicine [17] and interferon [12], still is controversial.

On the other hand, investigations of wound healing have been thoroughly developed to elucidate most of the mechanisms involved in its different phases [11]. Since

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Neuber's [19] work in 1893, several techniques for reshaping scar defects by adipose tissue transfer have been described [18], but until the 1980s, plastic surgeons oriented their choice to different materials despite well-known complications. At the end of the 1970s, Kesselring [14] and Illouz [15] suggested a new surgical technique: liposuction.

Since 1980, several papers have highlighted different findings on transplantation of fat obtained by liposuction [2,7,9,16], but adipose cell vitality has been a controversial subject, with survival rates ranging from 30% to 70% [10,23,24]. In 1992, Coleman [6,7] first described a new technique for improving adipose cell survival. Currently, adipose tissue can be harvested easily with minimal trauma. Liposuction and fat injection are commonly used in different clinical contexts.

At the same time, fat has been investigated, and microstructural studies have been developed. Adipose tissue contains an extracellular matrix (e.g., collagens, laminin, fibronectin, growth factors) and cellular components (adypocytes and many other factors). Moreover, recent interest has focused on adipose stem cells, which are capable of differentiating into fat, cartilage, bone, muscle, or nerve. Although adipose stem cells show less potential than embryonic cells, they can be obtained more easily than cells harvested from bone marrow [26,27].

Recently, Rigotti et al. [21] achieved clinical improvement by lipofilling the mammary region for severe radiodermatitis after cancer ablation and radiation therapy. All the above quoted researchers are the theoretical bases of our study on the evolution of scars in burned patients treated with the lipostructure technique.

Materials and Methods

Three informed voluntary patients with mature and immature scars resulting from hemifacial second- and third-degree burns and several surgical procedures were selected and treated with lipostructure from December 2005 to June 2006. Anamnestic patient data are summarized in Table 1.

After clinical assessment and routine preoperative examinations, the patients were submitted to liposuction of the subumbilical area under general anesthesia used to avoid the potential influence of local anesthetic on tissues. The abdominal harvesting area was chosen because it is an easily accessible, soft adipose tissue reservoir. An adipose tissue sample of about 30 ml was obtained to provide the adipocyte-containing middle layer and hematic cells suspended in the plasma at the bottom. The adypocite cell fraction was isolated and injected by sharp 0.1- to 0.2-mm cannulas at the dermal–hypodermal junction in the scar areas. This surgical procedure was performed twice, with a 3-month interval between procedures, to renew the dermal–hypodermal junction with a consistent amount of adipocytes distributed over time.

Before the first surgical intervention, at the time of the second surgery, and 3 months after the second surgical treatment, punch biopsies were obtained from the scar areas and from the surrounding unaffected areas as a control (data not reported). Specimens were processed into paraffin and stained with hematoxylin eosin to show the architectural features of tissues, collagen deposition, and vascularity. Magnetic resonance scans of the head with contrast agent [13] also were performed. The same surgical procedure and examinations were performed again after 90 days.

Results

After two treatments and a 6-month follow-up period, the appearance and subjective feeling of the three patients suggested an effective role of lipostructure for the scars. A considerable improvement in the mimic features, skin texture, softness, thickness, and elasticity was observed. Figures 1, 2, 3, 4, show the evolution of the scars experienced by patient 2.

Histologic section images of the biopsy tissue from patient 2 (Fig. 5, 6, 7) show patterns of new collagen deposition, local hypervascularity, and dermal hyperplasia. The presence of annexial structures is nearly normal. Altogether, the architecture is more preserved than in scars resulting from burns.

The magnetic resonance scan showed mild asymmetries in soft tissues compared with the contralateral, unaffected side (Fig. 8). No irregularity of signal enhancement was found.

Table 1 Patient data

Patient	Cause of burn	Extent of burn	Age of burn (years)	Age at first treatment (years)
1	Alcohol fire	40% of face, hands, inferior limbs	31	33
2	Contact with incandescent grill	5% of left half-face	33	36
3	Petroleum fire	40% of face, trunk, all limbs	4	16

Fig. 1 Preoperative view 5 years after burn injuries showing hypertrophic scars and keloids

Fig. 2 View of the patient 8 years after burn injuries, after multiple surgical procedures, and before the first treatment with fat injection. Note the alar nose retraction remaining, skin texture, and color

Fig. 3 Postoperative view 3 months after the second treatment with fat injection. Note the further improvement of skin texture and correct repositioning of the alar nose

Fig. 4 Postoperative view at the same time as Fig. 3 showing improvement in skin softness

Discussion

Coleman's lipostructure technique is widely used by many surgeons worldwide. Fat is abundant, expendable, and easily harvested and contains a high yield of cells. In addition, a fraction of liposuction-obtained cells has multipotent cells capable of self-renewal and amenable to gene therapy [8,22]. Some recent studies have shown the considerable effectiveness of the lipostructure technique in revitalizing chronic vascular sores and radiodermatitis [21].

Mature scars resulting from severe burns imply particularly difficult circumstances in their treatment because of abnormal fibroplasia, hypertrophy, and keloids secondary

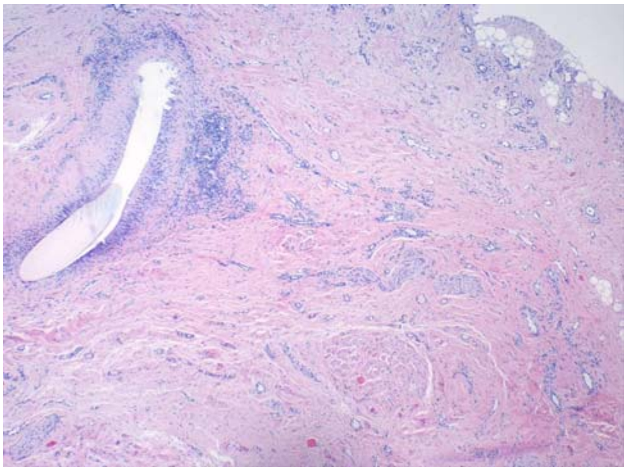

Fig. 5 Hematoxylin and eosin × 10 histological view of the scar area before fat injection. Note the typical appearance of the scar and the cellular necrosis around the hair follicle

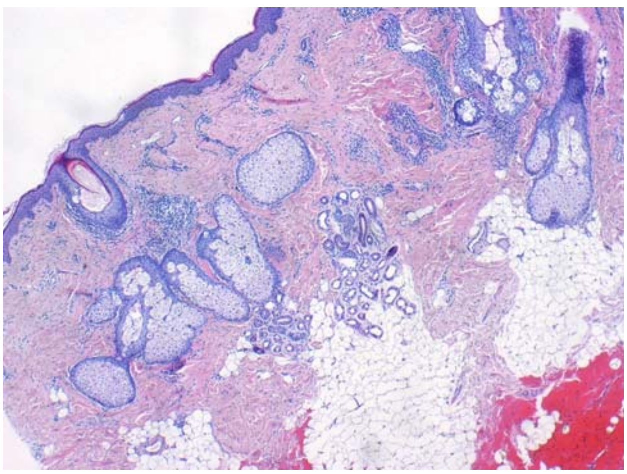

Fig. 6 Hematoxylin and eosin × 4 histologic view after the second treatment showing almost normal findings

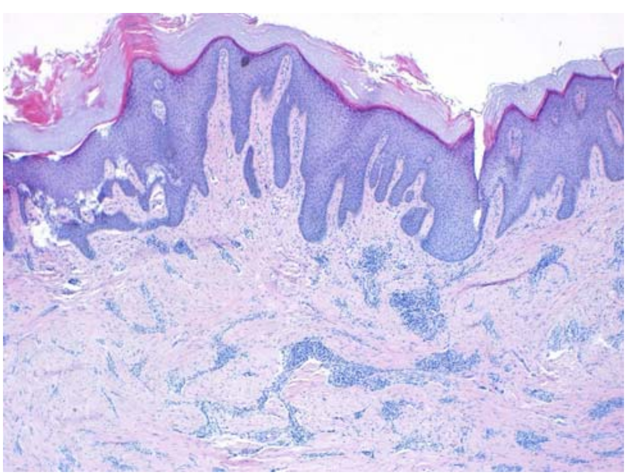

Fig. 7 Hematoxylin and eosin × 4 histologic view at the same time as the specimen shown in Fig. 6. Note the epithelial hyperplasia and neoangiogenesis

Fig. 8 Magnetic resonance scan of the head without contrast agent at the level of the superior alveolar arcades, performed at the same time as Figs. 3 and 4, showing similar signal enhancement of soft tissues on both the affected and the unaffected sides

to infections and inflammatory activity. Our clinical, magnetic resonance, and histologic findings show favorable results from our treatment of both mature and "evolving" scar tissue even in the case of severe, old burn outcomes. The pathophysiologic, cellular, and molecular mechanisms involved still have not been defined. Lipostructure at the dermohypodermal junction could increase the adipose layer widely destroyed by burn trauma and poorly regenerated during the reparative process.

The lipofilling procedure seems to improve the structural features of the extracellular matrix and increase its production. Autologous transplantation of stem cells present in the injected fat could account for this effect. This hypothesis is supported by Brzoska et al. [28], who reported epithelial differentiation of human adipose tissue–derived adult stem cells. Adult adipose stem cells represent a heterogeneous population with high variability depending on patient age, sex, and collection site, variables that can be crucial for cell therapy outcome. Characterization of the morphology and functionality of the subcutaneous abdominal adipose tissue before and after the implantation will provide some indications for performing a wider clinical trial as well as standard protocols for the therapy of severe burns and other pathologic scars.

Conclusions

The preliminary results suggest that lipofilling can improve scar quality. We speculate that this improvement depends on tissue regeneration promoted by adipose tissue–derived stem cells. The morbidity related to the procedure is minimal, similar to that for a limited liposuction, with acceptable safety. This result is encouraging and suggests further research to assess adipose cell properties, extracellular matrix composition, and the essential requisites for routine clinical applications.

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