FAT GRAFTS IN THE RECONSTRUCTION AND TREATMENT OF CHRONIC WOUNDS

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Transplantation of autogenic adipose tissue by means of the suction technique “anesthesia with edema”, has been for the past years one of the most engaged currents of contemporary plastic surgery. It is directly associated with the two issues described below. The first is the discovery of peripheral fat progenitor cells characterized by their in vitro plasticity (1). These cells are now referred to as Adipose Derived Stromal Cells (ADSC), being subjected to culture differentiation in different tissues, such as fat, cartilage, bone, or neural tissue (2). After isolation they may be applied in tissue engineering (3). Considering animal models they reveal interesting features, of which some have been described below. They can also be isolated in clinical conditions (4), as well as certified laboratories (5), and used as material in autologous fat grafting (6). Thus enriched fat tissue contains more ADSC, which is believed to help during the healing process after grafting. Autogenous fat grafts enriched with ADSC are currently the hottest topic considering plastic surgery conferences.

The second issue absorbing many researchers is the possibility to use fat tissue for the reconstruction of defects on the surface of the body. Attempts to fill subcutaneous tissue atrophy were made since the nineteenth century (7). However, their efficacy was considered questionable. Adipose tissue grafts are subject to rapid degradation and absorption. Recent years have brought a breakthrough in the above-mentioned area associated with changes in grafting techniques. Sydney R. Coleman, who in the late nineties of the past century observed that fat subjected to centrifugation administered in small doses might survive ischemia during healing, ultimately giving a lasting effect (8, 9, 10). The Author published his first studies in tandem with ADSC reports, which undoubtedly increased interest in his discovery. Over time, the above-mentioned also contributed to the increased interest in breast fat grafting.

Breast fat grafting

The filling and enlargement of breasts with the use of fat tissue, similarly to the filling of subcutaneous tissues located in other parts of the body has been practiced by many plastic surgeons, despite negligible effects. The early popularity of these methods was associated with the increased interest of esthetic fat tissue suction in the nineties of the past century. For obvious reasons, the transfer of fat from the abdomen or thighs to the breasts was enjoyed by many patients. The end of the popularity of breast enlargement using fat tissue was associated with the official position of the American Association of Plastic Surgeons (ASPS), considering the procedure as dangerous. This was connected with the increasing number of false-positive mammography results, where calcifying cysts were reported as tumors (11). ASPS sustained its position until 2009, when the report of the Task Force recognized that the current development of diagnostic methods enables to avoid erroneous descriptions (12). Allowing breast enlargement using fat tissue, ASPS sustained its precaution for some time, considering breast reconstruc-
ations by means of the above-mentioned method. The recent amendment introduces grade B recommendations, encouraging the use of available knowledge, remaining open to new evidence-based scientific data (13). Fat tissue breast reconstructions are currently performed in many worldwide leading centers, and thus, results may be assessed and reviewed.

Fat grafting techniques increase the efficacy of breast enlargement and reconstruction to such an extent, that in the near future these procedures might eliminate modern silicon prostheses. Amongst the described techniques one may distinguish three groups:

1. The first involves the use of modified Coleman’s technique, consisting in fat compaction by means of centrifugation, and small portion transplantation in the area of the pectoral muscle and subcutaneous tissue (14).

2. The second technique involves the use of fat tissue enriched with ADSC, which might be associated with increased efficacy (15).

3. The third technique prepares the breast for surgery by means of an external expander referred to as the BRAVA system (16).

Especially the latter method is characterized by high efficacy in case of reconstruction. The above-mentioned is associated with the need to provide a site for transplantation in the stretched subcutaneous tissue, and increased vascularization of the recipient site (16). Improved vascularization was confirmed by means of MRI in mice. The animals prepared for grafting by means of subcutaneous tissue stretching were characterized by increased subcutaneous tissue thickness after surgery, as compared to animals without the above-mentioned. Adipose tissue was characterized by increased vascular proliferation and remodeling, together with increased vascular diameters (17).

Some doubts are raised by the second of the presented techniques. Fat tissue enriched with ADSC might pose the risk of uncontrolled paracrine progenitor mesenchymal cell activity, and their potential susceptibility to metaplasia at the site of the removed tumor (18). It is emphasized that mesenchymal stem cells (MSC), derived from sources other than fat, have a proven tissue implantation ability. They tend to be found in the tumor stroma. After implantation they influence signaling pathways between surrounding mesenchymal and epithelial cells. This might lead to intercellular interaction disturbances at the site of metaplasia, which should raise suspicion (18).

Considering a recent study evaluating results obtained from 278 patients subject to breast reconstruction by means of fat grafting, after ten months of observation, 64 (23%) were diagnosed with a palpable lesion at the site of the operation. Seventeen patients underwent biopsy with recurrence confirmed in one case. The lesion was located outside the area of grafting. Independently, after three years of observation, three patients were diagnosed with metastases, 6 (2.2%) with local recurrence, and one died. The Authors came to the conclusion that the risk of local recurrence is within characteristics of patients who were not subjected to fat grafting (19). The recently published data might be evidence that in case of intraepithelial neoplasia the possible increased risk of local recurrence requires close follow-up and further clinical investigations (20). Principles of postoperative observation might be described on the basis of a simple management algorithm (19). Ultrasonography seems fundamental considering prophylaxis enabling to determine the character of most suspicious lesions (21). Therefore, despite the necessary precautions autogenous fat breast reconstructions will be performed more frequently. Especially, since the above-mentioned raises high hopes for the possibility of effective management considering patients with chronic thoracic wounds after radiotherapy.

Autogenous fat adjunctive to healing

Coleman’s studies were amongst the first to have highlighted the beneficial effect of fat grafting on the appearance and structure of the skin covering the graft. After the transfer of adipose tissue onto the dorsal surface of the aging hand, the Author observed the regression of senile and pigment lesions, improved thickening and structure of the skin, as well as the general influence on esthetics (22). Amongst other adipose tissue benefits the Author mentioned reduced tension and scar thickness, influence on healing post-radiation defects, chronic ulcerations, fibrous capsule contractures after endoprostheses reconstructions, and even vocal cord damage healing. ADS cells play a partial role in the above-mentioned (23).
The above-mentioned opinion was confirmed on animal experimental models. In case of rabbits, ADS cells increased the adhesion strength of the severed Achilles’s tendon, as compared to healing supplemented by platelet-rich plasma. The adhesions comprised an increased amount of collagen type I, FGF, and VEGF (24). In case of a rat model, considering healing of ischemic colonic anastomosis, ADSC increased vascularization, reduced weight lose of operated animals, as well as number of ulcerations and intestinal obstruction segments (25). Similar effects were observed in case of fat grafts without ADSC. In a mouse model of burn wounds, fat grafting was characterized by fast revascularization, and expression of proangiogenic proteins, such as VEGF. Fibrous scarring, determined on the basis of TGF-beta and metalloproteinase MMP9 expression proved to be weaker (26).

Similar results were obtained in the still small number of clinical investigations. In case of patients with long-lasting (several years) post-radiation ulcerations, ADSC cells implanted together with fat grafts increased the healing process. Results obtained in case of 10 elderly patients, determined on the basis of the clinical course, confirmed complete wound healing between the 2 and 10-th week after surgery. The Authors mentioned that complications were not observed, underlining the softness and structure of the healed skin (27). Similarly good results were presented after the treatment of post-radiation ulcerations by means of non-enriched fat grafts. Twenty female patients subjected to radiation after endoprostheses reconstructions underwent autogenous fat grafting. The clinical results confirmed improvement, as compared to patients without fat grafting. In case of four patients the fat graft above the prosthesis healed, while in those without fat grafts the implants were visible (28). In another group of 11 patients after radical oncological operations of the head and neck, fat tissue was administered for cosmetic effects, in order to improve the appearance of subcutaneous defects and scars. Long-lasting observations confirmed improvement in appearance, as well as healing of ulcerations and skin necrosis areas (29). Fat grafts can also be effective considering the treatment of post-burn deformations. Although existing literature data concerning the issue is scarce, the above-mentioned subject arouses increasing interest (30).

Detailed methodology concerning the treatment of ulcerations by means of fat tissue was published in an article, available to all. The Authors described a case of an 18-year old female patient, who as a result of a traffic accident, sustained left lower leg injuries, which healed with difficulty (31). The patient was initially treated by means of skin grafts, without no visible effect. Five months after the accident the Authors decided upon fat grafts. The grafts were collected from the hypogastrium using infiltration anesthesia. An angiographic needle was used (1.27 mm in diameter) instead of the standard cannula. The fat grafts were implanted into the wound and its edges. The Authors underlined the need to implant the adipose tissue in different directions and surfaces, as to increase contact with the granulation tissue. Three months after the operation the defect was healed. The final result which was confirmed by photographic documentation is evidence of the beneficial effect of fat tissue on the appearance and structure of the skin.

ADSC isolation and mechanism of action

Transplantation of fat-rich cells (cell-assisted lipotransfer) must be in accordance with the legal regulations concerning medical products and procedures. This is especially true in case of the US and European Union, where regulations sometimes render impossible the use of novel surgical techniques. Recently, an interesting study was presented concerning the compliance of enriching fat tissue with American law. In order to limit the processing of collected fat tissue to “minimal manipulation”, the Authors injected fat tissue and an enzyme releasing ADSC by means of separate subcutaneous injections (32). The enzyme isolated the cells just under the patients’ skin. Thus, one observed contracture release and softening of the scar. The Authors believe that the release of cells lead to their migration to the superficial layer, just under the skin, where they indonized and increased vascularization (32).

The molecular mechanism of ADSC activity remains unclear. According to the last prevailing theory the above-mentioned is as-
associated with their paracrine activity. Based on this theory, ADSC added to the portion of fat tissue influences vascular development in the vicinity of the graft. Thus, the vessels grow into the fat grafts. The activity of cells is limited to the production of bFGF, VEGF, PDGF and TGF-beta (33). This theory is in sharp contrast to the hypotheses, which assume that ADSC mesenchymal cells differentiate after transplantation into endothelial, smooth muscle cells, and pericytes. Very convincing evidence of such action have been shown on animal models. The Authors collected fat tissue from transgenic mice exhibiting simultaneous expression of luciferase and GFP. All cells obtained from such animals show green fluorescence. Thus, they are easily distinguished from mice cells, subjected to fat grafting (34). After 7 days, more ADSC cells were observed in adipose tissue pads subjected to experimental ischemia. After 14 days, more “non-illuminating” recipient vessels were observed. After 28 days, the fat tissue of ischemic pads ceased to atrophy. Moreover, proliferation was observed in case of recipient ADSC cells, instead of the “glowing” donor cells. Macrophages might also be responsible for the angiogenic effect of ADSC. According to the last reports, hypoxia in case of fat grafts is responsible for their recruration, stimulating the paracrine action (35).

REFERENCES

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