

Lipofilling in skin affected by radiodermatitis: clinical and ultrasound aspects. Case report

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SUMMARY: Lipofilling in skin affected by radiodermatitis: clinical and ultrasound aspects. Case report.

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In recent years, lipofilling has established itself as one of the most effective and least invasive techniques to treat connective dystrophy subsequent to radiotherapy. We report the case of a patient diagnosed with intraductal carcinoma of the right breast in 1996, at the age of 41. The patient underwent quadrantectomy with ipsilateral axillary lymph node dissection and adjuvant chemotherapy and radiotherapy. Four years later, a recurrence led the patient to undergo a subcutaneous mastectomy and immediate reconstruction, involving the submuscular insertion of a permanent implant. In 2007 the patient suffered both radiodermatitis and capsular contracture around the implant, causing constant pain and significant functional limitation. She first took a leukotriene inhibitor (Zafirlukast, 20 mg daily for 8 months) to reduce the capsular contracture. She then underwent lipofilling (Coleman's technique) of the area affected by radiodermatitis, in which the skin was considerably thinned and visibly ischemic. A second session followed four months later. Clinical, photographic and ultrasound examination revealed clear and lasting thickening of the superficial tissues, increased coverage of the implant, and reduced skin discoloration and tension.

RIASSUNTO: *Lipofilling* su cute irradiata: aspetti clinici ed ecografici di un caso trattato.

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Da alcuni anni una delle tecniche più efficaci e meno invasive per trattare distrofie del connettivo successive alla radioterapia è il lipofilling. Viene presentato il caso clinico di una paziente a cui nel 1996, all'età di 41 anni, era stato diagnosticato un carcinoma intraduttale della mammella destra. La paziente era stata quindi sottoposta a quadrantectomia con linfadenectomia ascellare omolaterale, chemio- e radioterapia adiuvanti. Dopo quattro anni, a causa di una recidiva di malattia, la paziente è stata sottoposta a mastectomia sottocutanea con ricostruzione immediata tramite inserimento sottomuscolare di protesi a permanenza. Alla fine del 2007, oltre la radiodermite, presentava una contrattura capsulare della protesi, tale da provocare sintomatologia dolorosa costante e forte limitazione funzionale. Il trattamento iniziale proposto è stato quindi di tipo farmacologico, con inibitore dei leucotrieni (Zafirlukast) 20 mg/die per 8 mesi; una volta ridotta la contrattura, l'area di cute radiodermatica, fortemente assottigliata e visibilmente ischemica, è stata trattata con due sedute di lipofilling secondo tecnica di Coleman. Tra la prima e la seconda seduta sono trascorsi quattro mesi. Il miglioramento, documentato clinicamente ed ecograficamente, è consistito in un ispessimento evidente e duraturo dei tessuti superficiali trattati, con aumento della copertura della protesi, miglioramento delle discromie cutanee e diminuzione della sensazione di tensione cutanea.

KEY WORDS: Breast - Cancer - Reconstruction - Radiodermatitis - Lipofilling, Mammella - Carcinoma - Ricostruzione - Radiodermite - *Lipofilling*.

Introduction

Numerous diseases of the connective and superficial tissues will at some point lead to a need for tissue re-creation, to help patients have a normal social life and achieve acceptance of themselves and their condition.

Atrophy or dystrophy of the superficial tissues is a common clinical event in various congenital, genetic and acquired diseases. Radiodermatitis is often found in cancer patients undergoing radiotherapy. This condition can be successfully treated through the implantation of autologous adipose tissue, known as lipofilling. This constantly improving technique, first developed in 1997 by the American surgeon S. Coleman (1), is the result of more than a century of attempts to transplant adipose tissue (2,3). Adipose tissue is in fact an ideal filler, as it is totally biocompatible (as it is an autologous tissue), readily available, inexpensive, and enables good aesthetic results (4-6). These features make it preferable to other injec-

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table materials such as synthetic, organic and homologous substances (3).

However, transplanted adipose tissue does not just restore volume. Until a few years ago, there was no known treatment for connective tissue diseases or of the effects of radiodermatitis. The improvement in skin tropism following transplantation of adipose tissue was a totally unexpected, chance discovery resulting from clinical observation of procedures performed for aesthetic purposes. The spread of the technique has revealed its enormous regenerative effect on the damaged tissues (7-9). These empirical observations led to a series of trials around the world to study the characteristics of adipose tissue (7-9). An initial literature review showed a large number of cells positive for CD24, CD9, CD105, CD73, CD106 (VCAM-1), CD29, CD44, CD90 and CD34 in the stromal fat sediment, as found in many stem cells. CD34+ cells probably correspond to the preadipocytes, which have a high replication rate and produce a large amount of matrix proteins (8,9). 1 gram of fat tissue can produce about 5,000 stem cells: 500 times more than the mesenchymal stem cells present in 1 gram of bone marrow (10-12).

The main limitation of this technique is the variable duration of the results. There is currently great interest in identifying factors affecting the duration. The sampling technique, the way the aspirated tissue is handled before injection, and the implantation technique used all have an effect (4,13-15). This explains why some authors (16) in the international literature report an almost complete resorption of adipose tissue in the months following surgery, while others note its almost total persistence. We generally find a certain degree of resorption (20-30%), so our injection technique is always hyper-corrective. Coleman recommends subsequent lipofilling sessions, to support the cumulative benefit of cell engraftment (17).

In recent years, the Department of Plastic, Reconstructive and Aesthetic Surgery of the "Sapienza" University of Rome has tried to standardize the most suitable technique for volume correction following superficial tissue dystrophy as well as to establish a procedure to repair damaged tissue, especially skin affected by radiodermatitis. We report the case of a woman treated with two sessions of lipofilling 4 months apart for radiodermatitis subsequent to breast cancer treated by radiotherapy and breast implants.

Case report

In June 1996 the patient, then aged 41, underwent a right breast quadrantectomy with ipsilateral axillary lymphadenectomy due to an infiltrating ductal carcinoma. The surgery was followed by a cycle of radiotherapy and two cycles of adjuvant chemotherapy. In July 2000 local recurrence led the patient to undergo a right subcutaneous mastectomy with submuscular placement of a breast implant and adju-

vant chemotherapy. Over the next two years, she underwent three operations for scar revision affecting the lower pole of the right breast, but the results were poor due to progressive tissue sclerosis caused by radiotherapy.

In December 2007 the patient, now aged 52, came to the Department of Plastic, Reconstructive and Esthetic Surgery of "Sapienza" University of Rome with severe dystrophy and pain due to significant capsular contracture of the right breast implant, for which she had been making chronic use of painkillers. The skin of the periareolar region and lower quadrants of the right breast was discolored, dystrophic and hypomobile, with thickness and temperature much lower than the corresponding contralateral areas.

Following her informed consent, the patient underwent an initial cycle of 8 months of treatment with a leukotriene inhibitor (18-20) (Zafirlukast, 20 mg per day) to reduce capsular contracture and pain. Following the success of this treatment, we then suggested the removal of the prosthesis and breast reconstruction with autologous tissue. This was refused.

The patient later underwent two sessions (February and June 2009) of Coleman lipofilling of the right breast, with the dual aim of improving skin tropism and increasing its thickness in the areola region and lower quadrants. Both sessions were conducted under local anesthesia with sedation. In the first session, the abdomen was chosen as the donor area and in the second, the adipose tissue was harvested from the hips and peri-trochanteric areas, to improve the patient's body contours. The harvested tissue was transferred in 10 cc Luer-Lok syringes and centrifuged at 1000/2000 rpm for 3 minutes. The plasma and blood layers and the oil from damaged cells were removed with further purification. The purified fat was then implanted with Coleman's cannulas, inserted through small incisions (1-2 mm) in the selected areas.

About 50 ml of purified fat was injected in the first session and about 70 ml in the second. The cannula entry points were sutured and a mildly compressive dressing applied to the lipofilled area for about one week. In the donor sites, the compressive dressing was left in place for two weeks. For three weeks thereafter the patient wore class II compression stockings during the day.

Focused ultrasound examinations were performed to assess the thickness between the epidermis and the outer limit of the peri-prosthetic capsule.

Periodic ultrasound examination revealed changes in the thickness of the subcutaneous tissue, while increased perfusion in the lipofilled areas was observed with power Doppler (Fig. 1).

Analysis of the data reported in Table 1 shows that the implanted tissue was never completely absorbed. Two months after the first session, the overall increase in the thickness of the treated areas was 228.57% (Fig. 2 a-b). Immediately prior to the second session (Fig. 2 c), the thickness had dropped to 114.29% of the baseline, demonstrating implanted tissue resorption of 50%. Two months after the second session, there was a 160% increase in the overall thickness compared to the baseline. This confirms the cumulative effect of multiple lipofilling sessions (8,17). The greatest resorption was in the lower outer quadrant of the right breast (right LOQ), the main area affected by chronic radiodermatitis.

Clinically, the tissues showed a steady improvement, with the color and temperature ever closer to that of the surrounding healthy skin. On palpation the skin also appeared significantly thicker and more mobile in comparison with the initial examination. The skin of the right submammary sulcus, which was initially fibrous and strongly adherent to the underlying tissues, was now easy to pinch. The discomfort originally reported by the patient had diminished to the extent that she felt no need for the final scheduled session.

A follow-up examination 21 months after the second session showed enduring tropism, and the increased softness of the treated tissue could be perceived from the improved profile of the lower breast (Fig. 2d).

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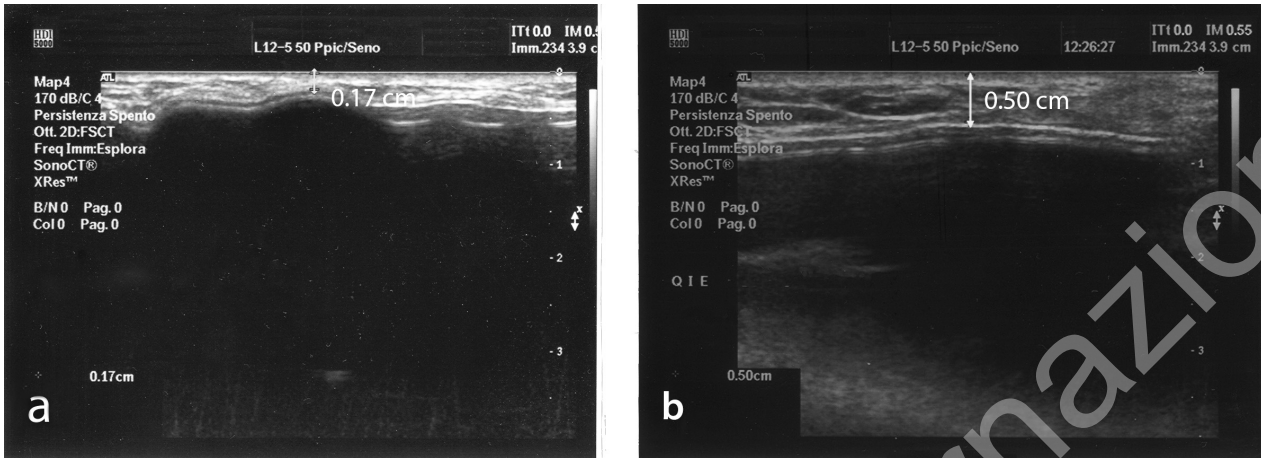


Fig. 1 - Ultrasound images: lower outer quadrant (LOQ) of the right breast a) prior to treatment and b) 3 months after first lipofilling session. The ultrasound examinations were performed by the same operator, using ATL Ultrasound HDI-5000.

TABLE 1 - VARIATIONS IN SUBCUTANEOUS THICKNESS ON ULTRASOUND EXAMINATION.

	APD R UOQ	APD R LOQ	Right under-areola region	Right sub-mammary sulcus
US baseline	0.30 cm	0.12 cm	0.18 cm	0.10 cm
US 2 months after 1 st lipofilling	0.64 cm	0.50 cm	0.59 cm	0.57 cm
US 4 months after 1 st lipofilling/prior to 2 nd lipofilling	0.42 cm	0.17 cm	0.41 cm	0.50 cm
US 2 months after 2 nd lipofilling	0.50 cm	0.33 cm	0.48 cm	0.51 cm

US = ultrasound; APD = anteroposterior distance between the outer edge of the periprosthetic capsule and the skin surface; UOQ = upper outer quadrant; LOQ = lower outer quadrant. All ultrasound examinations were performed by the same operator using ATL Ultrasound HDI-5000.

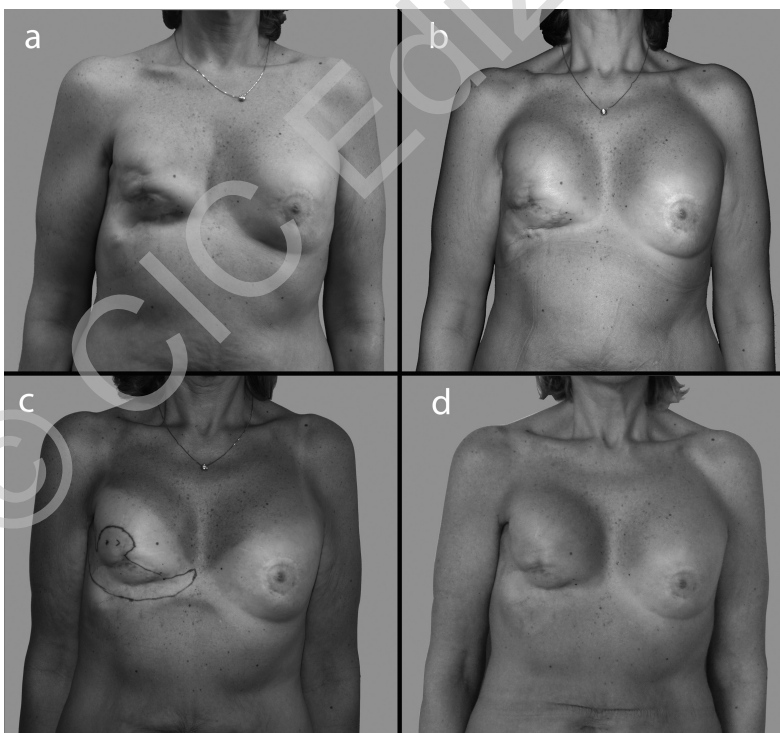


Fig. 2 - a) Pre-treatment: clear depression of the lower pole of the right breast, that is discolored and retracted at the scar of the previous quadrantectomy, axillary dissection and radiotherapy. b) Two weeks after the first lipofilling session: clear overall improvement in the lower pole. c) Four months after the first session, ready for the second session. There is still evident thickening of the superficial tissues of the LOQ and the right mammary sulcus and an improved breast shape. d) Follow-up 21 months after the second session: almost complete maintenance of the result.

Discussion

Radiotherapy is essential to “sterilize” any residual neoplastic foci after surgery as well as in cases of metastatic disease. The dose used is generally about 50 Gy if the disease is subclinical, and 60 Gy or more in the presence of a macroscopic residual in the operative site (21). However, side effects include radiodermatitis of healthy tissues. This normally affects the keratinocytes and is associated with erythema, scaling and edema, gradually progressing to fibrosis of the subcutaneous tissue and, in severe cases, to radionecrosis, in which the massive dose of ionizing radiation causes cell death and destruction. Melanocytes are also affected, resulting in skin discoloration (8).

The pathogenetic hypotheses advanced to explain this pathological progression focus on the role of the vascular component of the irradiated tissue: the vessels become hyper-permeable, leading to changes in local blood flow. Ultrastructural analysis by Rigotti et al. revealed clear signs of ischemia in relation to a microangiopathy, with a reduction in capillaries and visible duplication of the basal membrane. There was ectasia of the vessel lumen and endothelial cell activation, as demonstrated by the abundant cytoplasm and the presence of micropinocytotic vesicles. A space between the endothelial cells and pericytes was always visible and the adipocyte lysosome was damaged. Deposits of collagen and cellular debris consisting of fragments of membrane and external lamina were seen in the connective tissue, suggesting adipocyte rupture (8).

Chronic ischemia is the rationale for the application of treatment with pre-adipocytes, which induce angiogenesis and regenerate the damaged tissue with a lower intercellular fibrotic component. Stem cells from adipose tissue are in fact able to express various adhesion molecules and secrete important growth factors such as VEGF (vascular endothelial growth factor), PDGF- (platelet-derived growth factor-), HGF (hepatocyte growth factor), FGF-2,16,5,6 (2,16,5,6 fibroblast growth factor) and IGF-1 (insulin-like growth factor-1) (22,23). They are also able to maintain the proliferative pool at the recipient site, thanks to the asymmetric division characteristic of stem cells, providing a longer-lived graft (24). These events can be seen both ultrastructurally in biopsies performed during follow-up and clinically, with progressively improved quality and tropism of the tissue treated with lipofilling. According to some authors, these data suggest that the mechanism underlying ischemic lesions of radiodermatitis is very similar to the pathogenesis of scleroderma (8,9).

Conclusions

Ultrasound examination of the treated tissues during follow-up enabled us to document a real, persistent increase in subcutaneous thickness and improved vascular blood flow, confirming the validity of the transplantation of autologous adipose tissue in the treatment of skin with radiodermatitis.

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