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## Autologous adipose tissue graft in the vulva in severe vulvar lichen sclerosus atrophicus: clinical case

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### EXTRACT

**Introduction:** Vulvar lichen sclerosus atrophicus is a fairly widespread degenerative disease that significantly affects patients' quality of life. Symptoms are characterised by dyspareunia and vulvar atrophy, and are often associated with chronic pelvic pain, vulvodynia and vestibulodynia. From a pathogenic point of view, being a disease that predominately affects the skin layer, it is also classified as an atopic dermatitis dermatological disease, with a progressive thinning of skin thickness, loss of elasticity and appearance of abrasions and surface lesions. Its pathogenesis is unknown, but it is classified among the immune aetiology diseases; it appears to be more common in patients with viral infections, rheumatic diseases and endometriosis. Traditional treatments consist of local applications of cortisone-based creams and/or ointments on a cyclic 15-2-day basis, testosterone propionate at 2%, vitamin E and local oestrogens. Medical treatment is often not enough and exacerbations of the disease may occur.

**Clinical Case:** 66-Year-old patient suffering from vulvar lichen sclerosus atrophicus for several years with inability to have sexual intercourse due to dyspareunia, dysuria resulting from abraded skin coming into contact with urine and pain accompanied with rheumatic disease. Already treated for approximately 18 months with cortisone-based local therapies through a traditional regime on alternate days for 3 months with intervals of 2 months, followed by testosterone propionate at 2% and Vitamin E, as well as local hormone therapy and systemic therapy with vitamin A. Given the persistence of the symptoms and the resistance to pharmacological therapies, as well as the worsening of local symptoms with abrasions of the fourchette and labia minora, with an initial fibrous retraction of the vulva and perianal skin, with the classic figure-of-eight lesion (see photo 1), the patient was subjected to a vulvar biopsy, which resulted negative for neoplasms.

The patient accepted to undergo an innovative therapy involving the transplant of mesenchymal stem cells (taken from the autologous adipose tissue) implanted into the vulvar area, with the aim of promoting cell proliferation and differentiation, as well as stimulating neovascularisation of the area affected by a chronic degenerative process. In May 2016, under local anaesthesia, the patient underwent the lipoaspiration of the autologous adipose tissue from the abdomen and the processing of the cell material via a non-enzymatic technique (Lipogems®). Mesenchymal stem cells were then injected into the vulva, predominantly in the most affected areas, such as the fourchette, the labia minora and the periclitoral region in the same site. The patient was discharged within 24 hours without any post-operative nor remote complications. The rapid improvement occurred just 15 days after treatment. Subjectively, the patient reported having no dysuria due to the absence of abrasions, no vulva pain on simple touch and, objectively, the local department reported an absence of lesions on the fourchette, no perivulvar or perianal fibrous retraction, pink skin colour and softness of vulvovaginal tissues.

**Discussion:** The exclusivity of this clinical case lies in the fact that it is the first published case of the use of autologous adipose tissue transplant, processed using a non-enzymatic method, in the vulva in a patient with severe vulvar lichen sclerosus atrophicus. The rationale that led us to experiment with this procedure in vulvar lichen sclerosus atrophicus was to use the proliferative, differentiating, immunomodulatory features of stem cells that are necessary particularly for tissues affected by this highly debilitating disease. Mesenchymal cells are non-haematopoietic multipotent stem cells with the ability to differentiate, regenerate and repair various tissues such

as cartilage and bone, cardiac tissue and skeletal muscles, tendons and other tissues (e.g. adipose tissue). Mesenchymal cells have been identified in many tissues, such as bone marrow, adipose tissue, umbilical cord, dental pulp and the pulmonary epithelium. Umbilical cord tissue, dental pulp and adipose tissue are particularly rich sources of mesenchymal stem cells. Mesenchymal cells are the most studied adult stem cells, as they have peculiar characteristics in addition to those of stem cells derived from other tissues and organs. In addition, they can be easily isolated due to their ability to adhere to plastic and can be easily separated from other cells types due to the expression of a set of specific membrane markers. Furthermore, they can be easily expanded *in vitro* due to the high replicative potential, and have immunosuppressive and immunomodulatory functions via spontaneous migration to the tissues of origin and selective migration to damaged tissues (multiorgan homing capacity/trophism). In fact, mesenchymal cells, which are distinguished by their proliferative and immunosuppressive activity, are one of the main producers of exosomes (circular membrane fragments or microvesicles, with a diameter of 40–100 nm, released by the endosomal compartment or cell membrane), that are therapeutic in animals and have immunosuppressive and proliferative activities. It has also been hypothesised that the exosomes released by mesenchymal cells are one of the critical components in promoting self-renewal and expansion. They play a key role in cell-to-cell communication, through an interaction with their receptors or they can transfer, from the cell of origin, various bioactive molecules, including the exosomes secreted by the mesenchymal cells. They can induce or re-programme surviving cells from damaged tissue to re-enter the cell cycle and, therefore, promote the regeneration of the tissue. At the damaged site, they promote the regeneration of the affected tissue through differentiation and paracrine secretion of anti-inflammatory factors, marked functional plasticity and a multilineage differentiation potential, according to the new “developmental plasticity” theory, namely, the ability to cross the differentiation boundaries marked by the tissue they belong to. Adipose tissue processed using the Lipogems® method contains a significantly higher number of exosomes compared to the enzymatically processed tissue and this would explain its better efficacy. In fact, it enables to obtain tissue clusters that keep the cells in a more “native” environment, thus better supporting cell functionality, including the secretion of exosomes, important cell-to-cell communication mediators, in terms of proliferation, tissue regeneration and inflammation. On the contrary, the enzymatic treatment digests the extracellular matrix by affecting the secretory pattern, damages cells functionality and vitality, resulting in an excessively aggressive process, damaging the exosomes during processing. The tendency now is to use adult stem cells for both ethical issues, so as not to sacrifice an embryo and for oncological safety. They can also be used with total safety in autologous settings, ruling out the problem of immunological response and rejection.

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