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Dermatology Research

Efficacy of Subcutaneous Adipose Tissue Mesenchymal Stem Cell Therapy in Male Genital Lichen Sclerosus

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ABSTRACT

Background: *Lichen sclerosus (LS) presents a therapeutic challenge due to its chronic inflammatory nature, leading to sclerosis and atrophy, primarily affecting the anogenital region.*

Objective: *Stem cell therapy, particularly using subcutaneous adipose tissue-derived mesenchymal stem cells (AD-MSCs), shows promise due to their regenerative and immunomodulatory properties.*

Methods: *22 male patients with lichen sclerosus varying in degree from mild to severe were enrolled to undergo subcutaneous fat sampling using a sterile kit and subsequent processing of the stromal vascular fraction which was then freshly implanted in the same patients in an autologous manner.*

Results: *All patients reported a significant improvement in the signs and symptoms of the pathology already after a month and a half after therapy.*

Limitations: *This study is limited to a small group of male patients only.*

Conclusion: *Our data confirm the usefulness of this regenerative adipose tissue mesenchymal stem cells autologous transplant therapy in male genital lichen sclerosus.*

Keywords

Lichen sclerosus, Stem Cells, Autologous Mesenchimal adipose tissue Stem cells, Regeneration, Immunodermatology, General dermatology.

Capsule Summary

This article sheds light on ongoing regenerative therapies for lichen sclerosis, which are currently still stuck with high-potential steroids and topical immunomodulators.

In This procedure, the ease in carrying out, and the absence of adverse effects, can support any dermatologist, around the classic dermatological therapy in an innovative way.

- How does this article integrate into what was already known? This article sheds light on ongoing regenerative therapies for lichen sclerosis, which are currently still stuck with high-potential steroids and topical immunomodulators.
- How does it change practice? That is, what does the article mean to the practice of dermatology and what should you do as a result of having read this article? What should change in the way you practice? In This procedure, the ease in carrying out, and the absence of adverse effects, can support any dermatologist, around the classic dermatological therapy in an innovative way.

Introduction

Lichen sclerosus (LS) is a chronic inflammatory dermatosis characterized by sclerosis, atrophy, and significant discomfort, predominantly affecting the anogenital region [1]. Although LS is relatively rare, it can have profound physical and psychological impacts on affected individuals, particularly due to its chronic and often refractory nature [2]. Current therapeutic modalities, including topical corticosteroids and immunomodulatory agents, primarily

aim to alleviate symptoms and mitigate disease progression [3]. However, these approaches often provide only temporary relief and are associated with potential adverse effects, underscoring the need for alternative treatment strategies [4]. Stem cell therapy has emerged as a promising avenue in dermatology, offering the potential for tissue regeneration and immune modulation [5]. Subcutaneous adipose tissue-derived mesenchymal stem cells (AD-MSCs) have garnered particular interest due to their accessibility, abundance, and demonstrated therapeutic potential in various inflammatory and autoimmune conditions [6]. Preclinical studies have highlighted the immunomodulatory properties of AD-MSCs, including the suppression of pro-inflammatory cytokine production and promotion of regulatory T-cell differentiation [7]. Furthermore, AD-MSCs possess trophic and regenerative capabilities, secreting a myriad of growth factors and extracellular vesicles that facilitate tissue repair and regeneration [8]. Despite the promising preclinical data, clinical evidence supporting the efficacy of AD-MSCs therapy in LS management remains limited [9]. Few studies have explored the therapeutic potential of AD-MSCs in LS, and the existing literature primarily comprises case reports and small case series [10]. Therefore, there is a critical need for comprehensive clinical investigations to elucidate the therapeutic efficacy, safety profile, and mechanistic insights of AD-MSCs therapy.

In this context, we present a comprehensive case report analyzing the therapeutic outcomes of AD-MSC therapy in 22 patients diagnosed with moderate to severe LS. Detailed clinical assessments, including symptomatology evaluation and lesion severity scoring, were conducted pre- and post-treatment. Additionally, histological analyses were performed to assess tissue remodeling and treatment response. Our study aims to contribute to the growing body of evidence regarding the therapeutic potential of AD-MSC therapy in LS management and provide insights into its mechanistic underpinnings [11-14].

Materials and Methods

Before enrollment, patients provided written informed consent after receiving comprehensive information regarding the study objectives, procedures, potential risks, and benefits. The study protocol was approved by the institutional review board and conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

A clinical scoring system was the system for evaluating and collecting our cases of Lichen sclerosus, which we could briefly define as mild (10 patients) moderate (7 patients) and severe (5 patients) [15-17].

A histological examination of the area most affected by sclerosis was carried out for each patient in order to exclude cellular dysplasias and have histological confirmation of the diagnosis. Procedure: After the careful choice of the site of the sampling (usually abdominal adipose tissue, above the buttock or located on the hip), we proceeded, after careful disinfection, with superficial and deep anesthesia of the supra-fascial tissues. We then proceeded with a mini mechanical liposuction, using sterile disposable kits and a 16g needle of subcutaneous fat (approximately 7-10 cc of material); after collecting the material, the fat was washed and emulsified sterlilely. At the end, the fat was centrifuged using a sanitary centrifuge at 3000 rpm for 10 minutes. At the end of the procedure, the stromal vascular fraction was isolated in a sterile and purified manner and its subsequent arrangement inside Luer-Lock syringes with a 30 G needle. In the meantime, an anesthetic cream (Lidocaine-Prilocaine 2.5% - 2.5%) was applied to the patient at the site of implantation of the stromal vascular fraction, at the genital level. Therefore, the patient was able to receive the implantation of the stromal vascular fraction containing the mesenchymal cells derived from the subcutaneous fat in a completely painless way. After approximately 45 minutes, the procedure was completed and the patient was discharged after a check-up and prescription of antibiotic and anti-platelet drugs for a few days.

Clinical evaluations, included symptomatology assessment and lesion severity scoring, were conducted pre- and post-treatment.

Results

Analysis of 22 LS patients treated with AD-MSCs therapy revealed after 45 days, significant therapeutic benefits. Reduction in sclerosis (Figure 1A-B, 2A-B, 4A-B) and atrophy (Figure 1A-B,3A-B, 5A-B), resolution of cutaneous manifestations (Figure 1-5), and improvement in symptomatology, including pruritus and burning sensation, were observed post-treatment. Histological evaluations demonstrated favorable tissue remodeling and immunomodulatory effects, supporting the clinical findings.

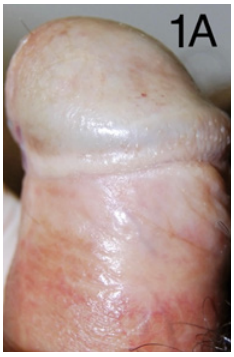

Figure 1A: Pre-therapy lichen sclerosus: note the porcelain white appearance of the mucosa and the mild sclerosis of the skin integument.

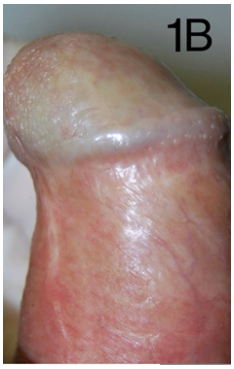

Figure 1B: Post therapy: normalization of the entire skin tegument with superficial revascularization and elasticization of the mucosa.

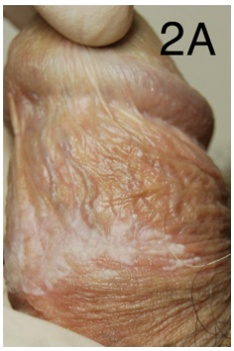

Figure 2A: Pre-therapy: presence of an imposing hyperkeratotic plaque corresponding to the ventral surface of the internal foreskin.

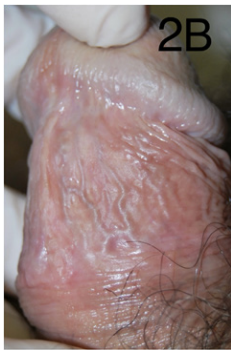

Figure 2B: Post therapy note the normalization of the ventral surface of the internal mucosa with complete disappearance of the porcelain white hyperkeratotic plaque from.

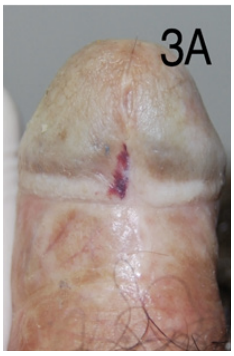

Figure 3A: Presence of atrophic stiffening of the mucosa associated with subcorneal ecchymosis (sign of progression of the atrophic phase of Lichen sclerosus).

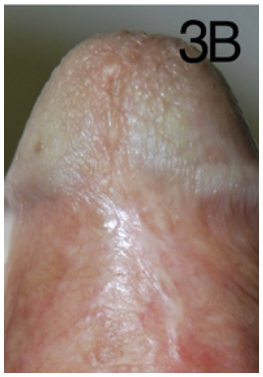

Figure 3B: Post therapy: elasticity of the entire mucosa with disappearance of the ecchymotic lesion

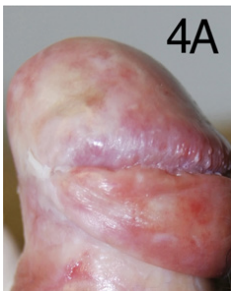

Figure 4A: Presence of diffuse tissue sclerosis with erosive lesions and hyperkeratotic plaque in correspondence with the frenulum.

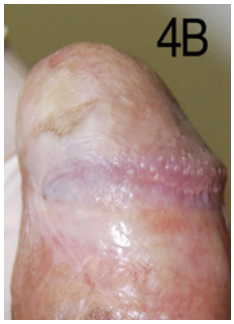

Figure 4B: Post therapy: normalization of the mucosa of the foreskin and the glans with disappearance of the erosions and the hyperkeratotic frenulum lesion.

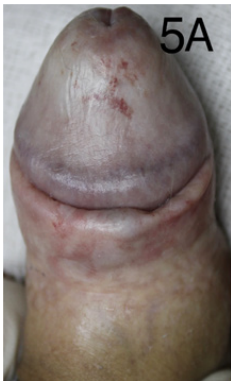

Figure 5A: Pre-therapy lichen sclerosus: note the inflammatory infiltrate associated with foreskin edema, micro fissures in the foreskin, atrophic areas and ecchymotic lesions of the glans.

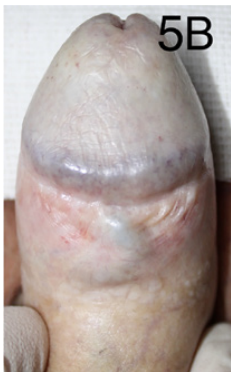

Figure 5B: Lichen sclerosus post therapy: note the normalization of the skin of the foreskin and the mucosa of the glans with disappearance of ecchymotic lesions and atrophic lesions of the glans, as well as micro fissures and preputial edema.

Discussion

The pathogenesis of LS involves complex interplay between genetic predisposition, autoimmune mechanisms, and aberrant extracellular matrix remodeling. Current therapeutic approaches primarily focus on symptom management, leaving a significant unmet need for disease-modifying treatments. Despite advancements in conventional therapies, sustained remission remains elusive. LS pathogenesis involves factors such as a genetic predisposition and an immune-mediated Th1-specific IFNγ-induced phenotype. Furthermore, there is a distinct expression of tissue remodeling associated genes as well as microRNAs. Oxidative stress with lipid and DNA peroxidation provides an enabling microenvironment to autoimmunity and carcinogenesis. Circulating IgG autoantibodies against the extracellular matrix protein 1 and hemidesmosome may contribute to the progression of LS

Current Therapeutic Paradigms

Conventional therapies for LS offer symptomatic relief but often fail to achieve sustained remission. Novel therapeutic strategies, such as stem cell therapy, are being explored to address underlying pathogenic mechanisms and promote tissue regeneration

Mechanistic Insights into AD-MSCs Therapy

AD-MSCs therapy offers a multifaceted approach by targeting inflammation, promoting tissue repair, and restoring immune homeostasis. Immunomodulatory effects, anti-fibrotic properties, and trophic support mechanisms contribute to the therapeutic efficacy of AD-MSCs in LS management

Clinical Implications and Future Directions

AD-MSCs therapy represents a promising therapeutic avenue for LS, offering potential disease modification and tissue regeneration. Future research should focus on optimizing treatment protocols, elucidating optimal dosing and delivery routes, and exploring long-term safety and efficacy profile

Conclusion

This case report highlights the therapeutic potential of AD-MSCs therapy in LS management. By addressing underlying pathogenic mechanisms and promoting tissue regeneration, AD-MSCs therapy offers a promising approach for improving outcomes and quality of life in LS patients. Further research endeavors are warranted to translate these promising findings into clinically applicable therapeutic strategies.

IRB approval status

Reviewed and approved by internal Institute IRB; approval #4.

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