Regenerative therapies in lichen sclerosus genitalis patients and possible efficacy in preventing squamous cell carcinoma development: a long-term follow-up pilot study

Marinella Tedesco,[1]* Barbara Bellei,[2]* Lavinia Alei,[1] Monia Di Prete,[3] Carlo Cota,[3] Tiziano Pallara,[1] Antonio Bonadies,[1] Alessandra Latini,[4] Stefania De Fazio,[5] Emilia Migliano[1]

[1]Department of Plastic and Reconstructive Surgery; [2]Laboratory of Cutaneous Physiopathology and Integrated Center of Metabolomics Research; [3]Genetic Research, Molecular Biology and Dermatopathology Unit; [4]Lichen Sclerosus Unit, Department of Dermatology, STI, Environmental Health, Tropical and Immigration, San Gallicano Dermatological Institute IRCCS, Rome; [5]International Liaison SICPRE, Italian Society of Plastic and Reconstructive Regenerative Surgery, Italy

*These authors contributed equally

Correspondence: Marinella Tedesco, M.D., Department of Plastic and Reconstructive Surgery, San Gallicano Dermatological Institute IRCCS, Via Elio Chianesi 53, 00144 Rome, Italy.
E-mail: marinella.tedesco@ifo.it
Tel.: +39 0652665438

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Abstract

Lichen sclerosus (LS) is a chronic scleroatrophic dermatosis of unknown etiology that usually affects the anogenital area and occasionally the extragenital sites, with no definitive cure. LS patients are at higher risk of developing squamous cell carcinoma (SCC) in their lifetime compared to the general population. Through a retrospective study, we evaluated the impact of regenerative medicine-based therapies on SCC onset in the context of genital LS. Patients with LS treated at our institute from March 2013 to December 2022 were reviewed. A total of 319 patients, including 34 treated with adipose-derived stem cell (ADSCs) grafts, 31 treated with ADSCs grafts and platelet-rich plasma (PRP), and 254 treated with PRP, were identified. In parallel, data extracted from the histologic institutional database, searching for SCC in the anogenital area, were matched to surgical records. None of the 319 LS patients developed skin SCC in the anogenital area. Our data suggest that cellular and acellular therapies achieving therapeutic control prevent continuous tissue remodeling and its evolution and, therefore, neoplastic degeneration. Regenerative approaches are considered a valid strategy for treating symptomatic LS patients despite prolonged first-line medical treatment. Studying the genital carcinogenesis of LS cases, we reported for the first time a protective role of PRP, ADSCs, and combined therapies. Thus, in terms of cancer prevention, we propose that regenerative therapies ameliorating disease control in non-responders to conventional therapy represent an important innovative tool.

Introduction

Several experimental and clinical shreds of evidence documented the possibility of potentiating intrinsic restorative and defense capacity through the regenerative medicine approach. Acellular therapies, which include the usage of stem cell-derived extracellular matrix, purified secreted vesicles, the entire secretome, platelet-rich plasma (PRP), and natural or synthetic polymers, aim to enhance tissue spontaneous restorative capacity. Cellular-based therapies involving graft-based mesenchymal stem cells (MSCs) significantly advanced the regenerative medicine field, given that these cells are non-specialized and have the ability to self-renew and differentiate into various cell types.[1] Thus, autologous stem cells sourced from disease- or injury-uninvolved tissue are useful to treat pathological conditions involving stem

cell exhaustion, as well as to accelerate natural tissue restoration. Among the several sources of MSCs, adipose-derived tissue stem cells (ADSCs) have garnered significant interest due to their extremely high number of staminal elements, regenerative capacities, ease of access, and immune-privileged setting.[2] However, it is important to take into consideration that a large proportion of the desired effects of stem cell therapy may be attributable to adipose tissue-derived secretome, containing many growth factors, lipids, and extracellular matrix components implicated in cell proliferation and tissue remodeling.[3] Moreover, since MSCs are immune-privileged cells that secrete a wide panel of cytokines, their ability to alter the host immune environment represents a promising treatment for inflammatory-associated diseases and autoimmune diseases.[4] Accordingly, very recently, the infusion of MSCs has been used to alleviate the non-protective cytokine storm of SARS-CoV-2 patients.[5]

Currently, regenerative approaches are considered a valid strategy for treating symptomatic lichen sclerosus (LS) patients despite prolonged medical treatment.[6] LS is a chronic, relapsing, inflammatory mucocutaneous skin disorder that usually involves the anogenital area. It is characterized by the appearance of ivory-white patches, ulcerations, ecchymosis, and atrophy with sclerosis. It can also result in the subversion of normal anogenital architecture, including fusion or loss of the labia minora, narrowing of the vaginal introitus, and burying of the clitoris, which can culminate in urinary and sexual dysfunction.[7] Genital dysplasia is frequent, and there is also an increased risk of squamous carcinoma of the penis and vulva.[8-10] The risk of anogenital squamous cell carcinoma (SCC) associated with LS corresponds to 2% for men.[9] Large epidemiological studies evidenced that women affected with vulvar LS have a lifetime risk of developing squamous cell carcinoma ranging from 2 to 7%. In comparison, up to 65% of vulvar carcinomas arise in a background of genital LS.[11,12] Additional evidence showed that the local recurrence of a vulval SCC is greater in patients with LS.[12] Some studies reported that SCC development is predominantly associated with female genital LS,[13] whereas others reported no gender differences.[14] The association with SCC seems to be very specific, since melanoma, basal cell carcinoma (BCC), and Merkel cell carcinoma are all sporadically reported in male and female patients with LS. Differently, SCC is not associated with extragenital LS.

Currently, treatment of LS is mainly initiated to relieve symptoms of pruritus and pain, to reduce the progression of skin alterations, and eventually to decrease the risk of cancer. Accepted first-line treatment of LS in the active phase consists of the daily local application of potent corticosteroids, mainly clobetasol propionate. In contrast, topical preparation of calcineurin inhibitors represents second-line treatment.[15] However, topical steroid therapy is not well-tolerated and successful in all LS patients. In general, adherence to prolonged topical therapy for cutaneous conditions is low.[16] Frequently, patients discontinue therapy for lack of rapid efficacy, resistance over time, or due to side effects (bacterial and fungal infection, thinning of the skin, dermal atrophy, dryness, telangiectasia, acne, and mild depigmentation).[17] Moreover, a small percentage of LS patients are resistant to topical steroid treatment. Nevertheless, the lack of a definitive cure for LS reflects the fact that the exact etiopathogenesis remains unknown. Immunological dysreactivity, chronic inflammation, and profibrotic activation of fibroblasts in the context of a susceptible genetic background are the major pathogenic mechanisms.[18]

For LS patients not responding to conventional pharmacological therapy, autologous ADSC transplantation and a combination of ADSCs and PRP demonstrated clinical improvement in most of the symptoms.[6,19] The biological rationale of PRP mixed with adipose tissue is based on the idea that PRP, being rich in several growth factors and cytokines, may contribute to fat graft survival.[20,21] Moreover, PRP modulates the immune system and extracellular synthesis, two altered conditions in LS. Accordingly, the injection of PRP alone also demonstrated significant clinical improvement in both male and female patients.[22] In this study, we analyzed the institutional patient database to evaluate the effects of regenerative therapeutic approaches (ADSCs, ADSCs combined with PRP therapy, or PRP alone) on the risk of genital LS progressing to SSC.

Materials and Methods

Patients' description

The study was approved by the institutional ethics committee. It was conducted in accordance with the Declaration of Helsinki, and informed consent was obtained from all patients. This retrospective research covered a nine-year period (2013-2022) at a single hospital. A total of 319 LS patients treated between March 2013 and December 2022 were identified through a retrospective review of electronic medical records. In particular, 34 patients were treated with ADSC grafts, 31 were treated with ADSC grafts *plus* PRP, and 254 were treated with PRP. These groups included patients still presenting symptoms due to poor corticosteroid efficacy, low compliance with therapy, or the relapsing nature of LS, causing a progression to severe late stages. All patients discontinued the use of topical steroids one month before and during the regenerative treatment period. Detailed methods for ADSC grafts and PRP injections were previously described.[20-22] In brief, patients underwent PRP infiltration three times at 15-day intervals. Sometimes, one or more additional treatments were repeated, with a minimum one-year interval between the initial infiltration. For the ADSC-based graft, the patient received two or three surgical procedures in a day-surgery regimen under general anesthesia, separated by four months. Adipose tissue was obtained from the abdominal area. Patient follow-ups ranged from 1 to 9 years. However, considering 5 years as a minimum period for cancer surveillance, a subset of patients presenting this characteristic was analyzed separately. The overall patient population consisted of 196 females and 123 males, with a mean age of 57.5±13 years (range 22-87 years). Anogenital SCC patients were extracted from the institutional database, considering the period 2013-2023.

Statistical analysis

Descriptive statistics were used to describe the patients' characteristics. Quantitative data were reported as mean±standard deviation (SD). The Student's *t*-test was used to assess statistical significance with thresholds of *p≤0.05 and **p≤0.01.

Results

The study included 319 consecutive cases of histologically proven penile and vulvar LS (mean age of 57.5±13 years; range 22-87 years) treated with regenerative medicine protocols in the Department of Plastic and Reconstructive Surgery at our institute. Gender distribution encompassed 196 females (mean age 58.8±12) and 123 males (mean age 53.8±14). In line with previous data reporting a significantly lower median onset age in males compared to females,[21] in this study, the gender-related age difference was statistically significant (p=0.000062) (Figure 1).

Here, patients were divided into three groups: Group 1 (n=254) being injected with PRP, Group 2 (n=34) receiving an autologous ADSCs graft, and Group 3 (n=31) receiving both treatments (Figure 2). Among the subjects included in Group 3, eighteen patients were injected with PRP and ADSCs during the same surgical event; of those, nine received additional PRP treatment during follow-up, four were enrolled for PRP injection and then received ADSCs grafts, and ten underwent ADSCs grafts and then received PRP during follow-up. Short-term (3 months) and longer-term (12 months) clinical follow-up confirmed previous data[6,22] concerning the effectiveness of treatments, which included symptom relief (itching, burning sensation, pain, and dyspareunia), as well as improvement in subjective findings (sexuality and quality of life) of patients (data not shown).

The median follow-up time was 4 years (mean 3.9±2.4 years; range 1-10 years), with the PRP group having a shorter post-treatment observation period (mean 3.3±1.8 years; range 1-9 years) than ADSCs (mean 5.8±3.1 years; range 1-10 years) and ADSCs plus PRP (mean 6.9±2.3 years; range 1-10 years). Patients receiving PRP and ADSCs in the same surgical event (n=18) have a longer clinical follow-up (8.5±0.55 years; range, 7-9 years), as this specific procedure is not yet used by our institute. A detail of the follow-up period distribution among different treatment regimens is reported in Figure 3. Further selection for a minimum follow-up period of 5 years (median, 7 years) resulted in 65 patients from Group 1, 23 patients from Group 2, and 25 LS patients from Group 3. Clinical observation showed that none of the 319 LS patients developed an SCC or other type of skin cancer in the genital area (113 subjects with at least 5 years of follow-up). By contrast, the analysis of data extracted from the histologic institutional database confirmed the frequent occurrence of SCC in the genital area of anogenital LS patients, since 18.5% of all anogenital SCC diagnosed between 2013 and 2023 presented genital LS. No difference in age or gender distribution was observed when comparing the groups of SCC without LS background and SCC with LS background (Table 1). However, none of the patients with SCC and a diagnosis of LS belonged to the group of patients treated with regenerative medicine therapies. The efficacy of regenerative treatments in SCC prevention is also indirectly reflected by the low percentage of anogenital SCC-LS (18.5%) among the entire anogenital SCC diagnosed in our institute. In fact, the literature reports a percentage of SCC occurring in LS background ranging from 31% to 86%.[11,13]

Discussion

LS is a rare disease with a great impact on the well-being and quality of life of affected subjects. LS causes anxiety and depression due to the diminished ability to perform daily activities of living and sexual dysfunction. Nevertheless, due to underreported symptoms by patients and the overlapping features with other dermatoses, the early diagnosis and treatment of LS are challenging. The delay of the initial diagnosis of LS impacts symptoms and the prognosis, including the probability of progression to SCC. Comparing gender differences, we observed a significantly lower median age for disease onset. However, we cannot rule out the possibility that differences in clinical presentation and subjective perception between genders may influence the timing of patients' presentation to the dermatology department, rather than reflecting a real difference in disease onset. Accordingly, using a two-stage classification, previous studies reported that more than 67% of female subjects arrive at the diagnosis at a late stage, whereas only 46% of males present late-stage characteristics at the first visit.[22,23] Early intervention with topical corticosteroids may prevent both scarring and tumor evolution in males and females.[24] However, compliance with therapy also plays a relevant role in SCC onset. Women compliant with topical corticosteroid treatment demon-

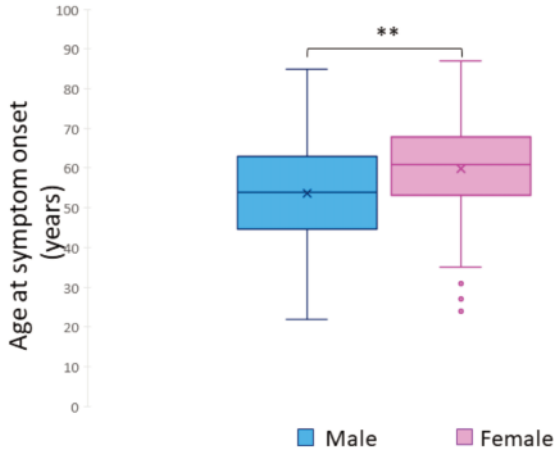

Figure 1. Plot of the difference in age. Age at the disease diagnosis was significantly lower in men compared to females (p=0.000062).

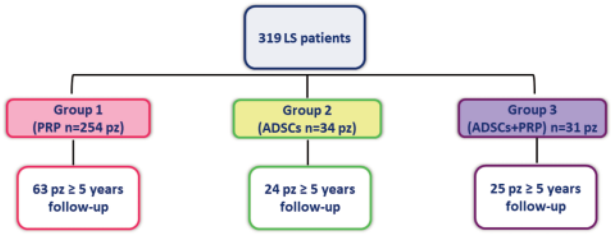

Figure 2. Graphical representation of patients' distribution according to the regenerative therapy used. The number of subjects with a minimal follow-up of 5 years is indicated in the lower boxes.

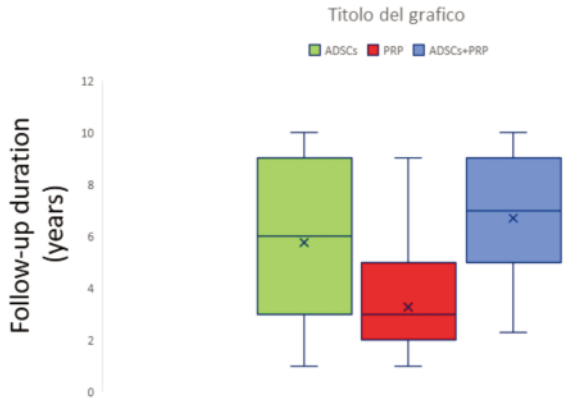

Figure 3. Plot of follow-up duration according to the type of regenerative therapy used.

Table 1. Anogenital SCC patients' characteristics. The table includes anogenital SCC diagnosed between 2013 and 2023.

	Age (mean±SD)	Age (range)	Male	Female	Number	%
SCC	65.6±14	29-93	94	54	148	81.3%
SCC with LS	78.1±11	40-91	26	8	34	18.7%

SD, standard deviation; SCC, squamous cell carcinoma; LS, lichen sclerosus.

strate lower rates of vulvar SCC compared to women who were inconsistent with this treatment.[25] Some patients prematurely discontinue therapy for lack of prompt efficacy or because of side effects. On the other hand, concerns about long-term corticosteroid use can undermine patient compliance and motivation. Thus, strategies recommended to minimize exposure to corticosteroids are needed for chronic skin diseases such as LS. Collectively, these studies suggest that considering the potential evolution towards cancer, LS needs to be treated, even when asymptomatic. Particularly, subclinical persistent inflammation engaging reactive oxygen species (ROS)-dependent tissue sclerosis and scarring might facilitate atypical hyperproliferative processes.[26] Due to the complicated pathogenesis, there is no definitive treatment strategy for LS patients. Ultrapotent topical corticosteroids' effectiveness lies in their anti-inflammatory effect *via* interaction with the intracellular glucocorticoid receptor and the immunosuppressive action. Still, clinical evidence of reduced dermal fibrosis[27] lacks a biological explanation. Other possible therapies sporadically used for LS patients, such as UVA1, microablative fractional radiofrequency, and topical retinoids, counteract the pro-fibrotic process, restoring normal collagen synthesis and metabolism.[28,29] Similarly, even if the loss of oxidative equilibrium is considered secondary to inflammation, direct targeting of oxidative stress by systemic or topical supplementation with vitamin E and other antioxidants is retained as a valid adjuvant option to prevent disease progression and transformation into carcinoma.[30]

A vast repertoire of experimental and clinical studies illustrated that regenerative therapies act on most of the LS pathogenic mechanisms. PRP is a blood product enriched in growth factors and cytokines, which promotes tissue regeneration, angiogenesis, and immune modulation. Clinical studies demonstrated the efficacy of stem cell-enriched fat grafting in reducing fibrosis, pain, burning, and dyspareunia and restoring anatomical and functional outcomes in both male and female LS patients.[31] Moreover, the combination of PRP and ADSCs seems to offer a synergistic approach to address the complex pathophysiology of LS, particularly in the early stages.[6] ADSCs' regenerative property relies not only on their cell replacement capacity but also on the secretion of trophic factors and modulation of the local immune response. Laboratory-based biological characterization of grafted material clearly showed that in addition to pluripotent cells, it contains direct ROS scavenger activity, stimulators of cell antioxidant endogenous capacity, immune-regulatory factors implicated in $CD8^+$ T cells proliferation and skin homing, and molecules involved in extracellular matrix remodeling,[2,32] explaining clinical shreds of evidence. Yet, questions regarding the oncological safety of therapeutic stem cells have been raised, as many components required for successful regenerative therapy, such as revascularization, immunosuppression, and cellular mobilization, are also critical for tumor onset and relapse. *In vivo* studies documented divergent results, showing a possible pro-carcinogenic risk in autologous adipose tissue-derived therapies,[33] as well as no increased risk of tumor recurrence in patient populations receiving adipose tissue-based intervention.[34] However, our and other previous *in vitro* studies documented that, in contrast to normal cells, the proliferation rate of cancer cells (including skin squamous carcinoma and melanoma cells) is not affected or, in some cases, negatively influenced by adipose tissue-derived stem cell secretome.[2,34] In line with these data, we reported that none of the LS patients treated with ADSCs, PRP, or ADSCs/PRP combined therapy developed SCC or BCC in the anogenital area during a medium-term follow-up, suggesting a protective role of these treatment options. The explanation could be the optimal control of disease symptoms or the intrinsic propensity of transplanted material to interrupt the chronic inflammatory state typical of the dermal and epidermal skin of affected subjects, as well as the marked capacity to re-equilibrate the oxidative equilibrium, since oxidative stress is deeply implicated in the carcinogenic process in LS.[35]

Conclusions

In conclusion, data regarding the usage of regenerative therapies for LS patients confirm the safety and efficacy of these treatments, encouraging further evaluation for cancer prevention. There is no doubt that disease control, particularly attenuation of the inflammatory cascade, acts to prevent the onset of genital SCC for patients with genital LS. However, the clinical data presented in this work suggest that regenerative medicine treatments, both surgical (ADSCs and ADSCs combined with PRP graft) and simple intradermal injection of PRP, have a strong impact on the restoration of physiological tissue balance and consequently on neoplastic evolution. The efficacy of regenerative treatments in SCC prevention is indirectly supported by the relatively low percentage (18.5%) of anogenital SCC cases associated with LS when considering the total number of SCC cases (both LS-associated and non-associated). This may reflect the routine use of regenerative medicine-based therapies in eligible LS patients at our institute. In fact, data from the literature describe the percentage of SCC-LS among the total number of SCC, ranging from 31% to 86%.[11,13] Beyond the biological mechanisms underlying this observation, it is possible that this therapeutic option is intrinsically more effective than delegating long-term home management to the patient. In terms of cancer prevention, this leads to a reflection on the expansion of the offer of regenerative therapies not only to patients who do not respond to conventional therapies.

References

1. Ong WK, Chakraborty S, Sugii S. Adipose tissue: Understanding the heterogeneity of stem cells for regenerative medicine. Biomolecules 2021;11:918.
2. Bellei B, Migliano E, Tedesco M, et al. Maximizing non-enzymatic methods for harvesting adipose-derived stem from lipoaspirate: Technical considerations and clinical implications for regenerative surgery. Sci Rep 2017;7:10015.
3. Aust L, Devlin B, Foster SJ, et al. Yield of human adipose-derived adult stem cells from liposuction aspirates.

Cytotherapy 2004;6:7-14.
4. Huang Y, Wu Q, Tam PKH. Immunomodulatory mechanisms of mesenchymal stem cells and their potential clinical applications. Int J Mol Sci 2022;23:10023.
5. Sadeghi S, Soudi S, Shafiee A, et al. Mesenchymal stem cell therapies for COVID-19: Current status and mechanism of action. Life Sci 2020;262:118493.
6. Tedesco M, Bellei B, Garelli V, et al. Adipose tissue stromal vascular fraction and adipose tissue stromal vascular fraction plus platelet-rich plasma grafting: New regenerative perspectives in genital lichen sclerosus. Dermatol Ther 2020;33:e14277.
7. Pugliese JM, Morey AF, Peterson AC. Lichen sclerosus: Review of the literature and current recommendations for management. J Urol 2007;178:2268-76.
8. Davick J, Samulson M, Krone JT, Stockdale CK. The prevalence of Lichen Sclerosus in patients with vulvar squamous cell carcinoma. Int J Gynecol Pathol 2017;36:305-9.
9. Virgili A, Borghi A, Cazzaniga S, et al. New insights into potential risk factors and associations in genital lichen sclerosus: Data from a multicentre Italian study on 729 consecutive cases. J Eur Acad Dermatol Venereol 2017;31:699-704.
10. Virgili A, Borghi A, Cazzaniga S, et al., Gender differences in genital lichen sclerosus: data from a multicenter Italian study on 729 consecutive cases. Italian Study Group. G Ital Dermatol Venereol 2020;155:155-60.
11. Spekreijse JJ, Streng BMM, Vermeulen RFM, et al. The risk of developing squamous cell carcinoma in patients with anogenital lichen sclerosis: A systematic review. Gynecol Oncol 2020;157:671-7.
12. Preti M, Borella F, Ferretti S, et al. Genital and extragenital oncological risk in women with vulvar lichen sclerosus: A multi-center Italian study. Maturitas 2023;175:107767.
13. Yap JKW, Fox R, Leonard S, et al. Adjacent lichen sclerosis predicts local recurrence and second field tumour in women with vulvar squamous cell carcinoma. Gynecol Oncol 2016;142:420-6.
14. Wang Y, Jin G, Li Q, et al. Hedgehog signaling non-canonical activated by pro-inflammatory cytokines in pancreatic ductal adenocarcinoma. J Cancer 2016;7:2067-76.
15. Lewis FM, Tatnall FM, Velangi SS, et al. British association of dermatologists guidelines for the management of lichen sclerosus, 2018. Br J Dermatol 2018;178:839-53.
16. Hougeir FG, Cook-Bolden FE, Rodriguez D, et al. Critical considerations on optimizing topical corticosteroid therapy. J Clin Aesthet Dermatol 2015;8:S2-14.
17. Renaud-Vilmer C, Cavelier-Balloy B, Porcher R, et al. Vulvar lichen sclerosus: Effect of long-term topical application of a potent steroid on the course of the disease. Arch Dermatol 2004;140:709-12.
18. Tran DA, Tan X, Macri CJ, et al. Lichen sclerosus: An autoimmunopathogenic and genomic enigma with emerging genetic and immune targets. Int J Biol Sci 2019;15:1429-39.
19. Monreal J. Safety and efficacy of stromal vascular fraction enriched fat grafting therapy for vulvar lichen sclerosus. Cureus 2020;12:e7096.
20. Rigotti G, Charles-de-Sá L, Gontijo-de-Amorim NF, et al. Expanded stem cells, stromal-vascular fraction, and platelet-rich plasma enriched fat: Comparing results of different facial rejuvenation approaches in a clinical trial. Aesthet Surg J 2016;36:261-70.
21. Peng Q, Zhao L, Hou Y, et al. Biological characteristics and genetic heterogeneity between carcinoma-associated fibroblasts and their paired normal fibroblasts in human breast cancer. PLoS One 2013;8:e60321.
22. Tedesco M, Garelli V, Bellei B, et al. Platelet-rich plasma for genital lichen sclerosus: Analysis and results of 94 patients. Are there gender-related differences in symptoms and therapeutic response to PRP? J Dermatolog Treat 2022;33:1558-62.
23. Latini A, Cota C, Orsini D, et al. Male and female genital lichen sclerosus. clinical and functional classification criteria. Postepy Dermatol Alergol 2018;35:447-53.
24. Neill SM, Lewis FM, Tatnall FM, et al. British association of dermatologists' guidelines for the management of lichen sclerosus 2010. Br J Dermatol 2010;163:672-82.
25. Lee A, Bradford J, Fischer G. Long-term management of adult vulvar lichen sclerosus: A prospective cohort study of 507 women. JAMA Dermatol 2015;151:1061-7.
26. Yu W, Tu Y, Long Z, et al. Reactive oxygen species bridge the gap between chronic inflammation and tumor development. Oxid Med Cell Longev 2022.
27. Dalziel KL, Millard PR, Wojnarowska F. The treatment of vulval lichen sclerosus with a very potent topical steroid (clobetasol propionate 0.05%) cream. Br J Dermatol 1991;124:461-4.
28. Gambichler T, Terras S, Kreuter A. Treatment regimens, protocols, dosage, and indications for UVA1 phototherapy: Facts and controversies. Clin Dermatol 2013;31:438-54.
29. Li HO, Bailey AMJ, Tan MG, et al. Lasers as an adjuvant for vulvar lichen sclerosus: A systematic review and meta-analysis. J Am Acad Dermatol 2022;86:694-6.
30. Russo T, Currò M, Ferlazzo N, et al. Stable ozonides with vitamin E acetate versus corticosteroid in the treatment of lichen sclerosus in foreskin: Evaluation of effects on inflammation. Urol Int 2019;103:459-65.
31. Tedesco M, Bellei B, Garelli V, et al. Adipose tissue stromal vascular fraction and adipose tissue stromal vascular fraction plus platelet-rich plasma grafting: New regenerative perspectives in genital lichen sclerosus. Dermatol Ther 2020;33:e14277.
32. Plumas J, Chaperot L, Richard M, et al. Mesenchymal stem cells induce apoptosis of activated T cells. Leukemia 2005;19:1597-604.
33. Freese KE, Kokai L, Edwards RP, et al. Adipose-derived stems cells and their role in human cancer development, growth, progression, and metastasis: A systematic review. Cancer Res 2015;75:1161-8.
34. Vyas KS, DeCoster RC, Burns JC, et al. Autologous fat grafting does not increase risk of oncologic recurrence in the reconstructed breast. Ann Plast Surg 2020;84:S405-10.