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Refractory Stasis Dermatitis Due to Chronic Venous Insufficiency With Psychosocial Worsening in 2 Septuagenarian Patients Treated With Hyaluronic Acid–Succinic Acid Intradermotherapy

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Case series

Patients: Male, 77-year-old • Female, 75-year-old

Final Diagnosis: Stasis dermatitis

Symptoms: Severe pruritus, pain, skin fissuring, and functional impairment, with associated psychological deterioration

Clinical Procedure: Intradermotherapy

Specialty: Dermatology

Objective: Unusual clinical course

Background: Stasis dermatitis is a chronic inflammatory dermatosis secondary to chronic venous insufficiency. Treatment of refractory cases remains challenging. High-molecular-weight non-crosslinked hyaluronic acid (HMWNCHA) combined with succinic acid (SA) possesses anti-inflammatory and regenerative properties. We report 2 septuagenarian patients with refractory stasis dermatitis and psychosocial deterioration treated with intradermal HMWNCHA plus SA.

Case Reports: Case 1 involved a 77-year-old man with chronic venous insufficiency and refractory stasis dermatitis associated with severe symptoms, impaired mobility, and psychosocial deterioration. After failure of conventional therapies, he received 2 sessions of intradermal HMWNCHA plus SA administered 1 month apart, resulting in marked and sustained clinical and psychosocial improvement at 6-month follow-up. Case 2 involved a 75-year-old woman with refractory unilateral stasis dermatitis secondary to chronic venous insufficiency. Following the same treatment protocol, substantial improvement was observed after the first session, with near-complete lesion resolution after the second session and sustained remission at 6-month follow-up. No treatment-related adverse effects were reported.

Conclusions: In these 2 patients with refractory stasis dermatitis, intradermal HMWNCHA plus SA was associated with marked and sustained clinical improvements and enhanced quality of life. Further studies are warranted to confirm these findings.

Keywords: Dermatitis • Hyaluronic Acid • Succinic Acid • Case Reports • Dermatology

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Introduction

Stasis dermatitis is an eczematous inflammatory disorder of the lower extremities secondary to chronic venous insufficiency. Characterized by pain, swelling, persistent pruritus, and ulceration [1], the condition imposes a significant physical burden, including sleep disruption, impaired mobility, and reduced capacity for daily activities [2]. Chronic venous insufficiency (CVI) is a common vascular disorder characterized by impaired venous return and venous hypertension, most frequently resulting from valvular incompetence, venous obstruction, or calf muscle pump dysfunction [3]. CVI affects approximately 10-35% of adults and may progressively lead to edema, skin trophic changes, stasis dermatitis, and venous ulceration, particularly in older individuals [4]. Stasis dermatitis represents one of the most common cutaneous manifestations of CVI and is characterized by erythema, scaling, pruritus, xerosis, pain, and skin barrier dysfunction resulting from chronic inflammation and microvascular alterations [5]. Diagnosis is based on clinical evaluation and is confirmed by venous duplex ultrasound, the current gold-standard diagnostic modality [6]. Management primarily focuses on addressing the underlying venous disease through compression therapy, leg elevation, exercise, skin care, and pharmacological or interventional procedures when indicated; however, refractory stasis dermatitis remains a significant therapeutic challenge [7]. These effects are compounded by profound psychological distress, leading to a marked decline in quality-of-life and social functioning, and a heightened risk of depression [6].

Geriatric psychodermatology is an emerging interdisciplinary field that explores the complex relationship between dermatological conditions and psychological health in older adults. Age-related skin changes, chronic dermatoses, pruritus, and visible signs of aging may significantly affect self-perception, emotional well-being, social functioning, and quality of life [8]. Conversely, psychiatric and psychosocial factors such as anxiety, depression, stress, cognitive impairment, and social isolation can influence the onset, severity, and progression of dermatological disorders. Given the bidirectional interaction between the skin and the nervous system, often referred to as the skin-brain axis, comprehensive management of patients of advanced age may benefit from an integrated approach that addresses both cutaneous and psychological aspects of health [9].

Despite the high prevalence and considerable clinical impact of stasis dermatitis, there are currently no specifically approved or consistently effective therapies for managing this condition [10]. The combination of high–molecular-weight non-crosslinked hyaluronic acid (HMWNCHA) and succinic acid (SA) has been shown to exert anti-inflammatory, pro-regenerative, and bacteriostatic effects [11]. This combination, also referred to as redermalization, is a minimally invasive injectable treatment involving the administration of bioactive compounds into both the dermis and superficial subcutaneous tissue. Originally developed for skin rejuvenation and the management of age-related dermal changes, this approach has demonstrated biostimulatory, regenerative, anti-inflammatory, and antioxidant properties [12]. HMWNCHA contributes to tissue hydration, extracellular matrix homeostasis, and wound repair, whereas SA supports cellular metabolism and mitochondrial function [13]. Recent evidence suggests that the combination may promote dermal regeneration, improve skin quality, and modulate inflammatory responses [14], expanding its potential applications beyond aesthetic medicine to inflammatory and chronic dermatological conditions.

The aim of this report is to describe the clinical outcomes in 2 septuagenarian patients with refractory stasis dermatitis and psychosocial deterioration treated with intradermal microinjections of HMWNCHA combined with SA, and to explore the potential therapeutic role of this approach in improving cutaneous and patient-reported outcomes.

Case Reports

Case 1

A 77-year-old White man presented with a 1-year history of progressive severe pruritus, pain, and impaired mobility due to stasis dermatitis. The patient did not present hypertension, obesity, or associated metabolic pathologies.

Physical examination revealed erythematous-violaceous patches with marked xerosis and fissuring on both lower legs, with no fever or systemic signs of infection. CVI had been previously diagnosed by Doppler ultrasound and managed conservatively; Daflon 500 mg 2 times per day (Escin, micronized purified flavonoid fraction), compression stockings (20-30 mm Hg), leg elevation, and exercise, with no surgical intervention indicated.

Laboratory evaluation showed elevated C-reactive protein levels (0.52 mg/dL) without other abnormalities. After failure of topical clobetasol (0.05%, night use) followed by tacrolimus (0.1%, night use) combined with oral levocetirizine (5 mg every night), the patient developed significant psychological deterioration, including depressive symptoms and suicidal ideation, and was referred to psychiatry. He subsequently underwent intradermal microinjections of HMWNCHA combined with SA (Xela Rederm 1.8% 2 mL, class III injectable medical device delivering 18 mg/mL of HMWNCHA and 16 mg/mL SA, CE #0373 and Instituto de Salud Pública (Chile) approved, Institute Hyalual Ltd., Switzerland, produced by Diaco Biopharmaceutical, Italy), administered in 2 sessions 1

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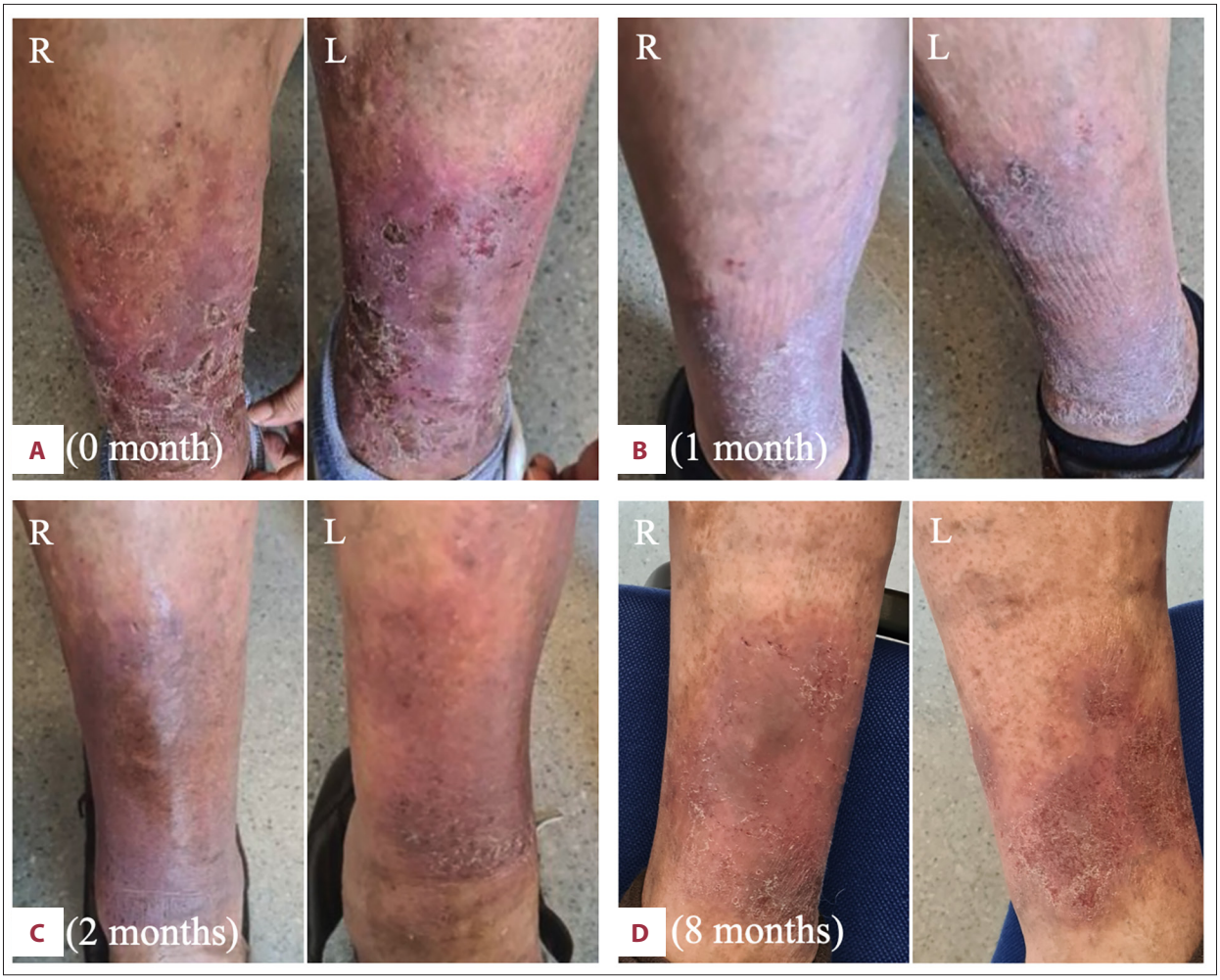

Figure 1. Clinical improvement of bilateral stasis dermatitis following intradermotherapy with HMWNCHA and SA in Case 1. Serial clinical photographs of a 77-year-old male patient with bilateral stasis dermatitis treated with intradermal microinjections of HMWNCHA combined with SA. (**A**) Baseline presentation showing erythematous-violaceous patches, marked xerosis, and skin fissuring affecting both lower legs. (**B**) Clinical appearance 1 month after the first treatment session, demonstrating improvement in skin hydration and reduction of erythema. (**C**) Clinical appearance 1 month after the second treatment session (2 months after treatment initiation), showing further improvement in skin quality and lesion severity. (**D**) Six-month follow-up after the second treatment session (8 months after treatment initiation), demonstrating sustained clinical remission and restoration of skin integrity. R, right leg; L, left leg; HMWNCHA, high-molecular-weight non-crosslinked hyaluronic acid; SA, succinic acid.

month apart. Marked improvement in skin quality (**Figure 1**), neurosensitive symptoms (**Figure 2**), mobility, and mood was observed after the first session, with sustained remission at 6-month follow-up on emollient therapy alone.

Case 2

A 75-year-old White woman with hypertension and dyslipidemia, treated with losartan (50 mg twice daily) and atorvastatin (20 mg daily), presented with an erythematous macular lesion on the left ankle associated with severe pruritus, mild pain, and swelling. Doppler ultrasound confirmed unilateral CVI affecting the involved limb, which was managed conservatively; surgical or sclerotherapy options were not indicated. The specialist prescribed Daflon 500 mg 2 times per day (Escin, micronized purified flavonoid fraction), compression stockings (20-30 mm Hg), leg elevation, and exercise.

After failure of topical clobetasol followed by tacrolimus combined with oral levocetirizine, the patient started presenting mobility problems, associated with persistent pruritus, sleep disturbance, and skin fissuring with occasional bleeding, aggravated by friction from socks and footwear. She was treated using the same intradermal microinjection protocol of HMWNCHA combined with SA as in Case 1. Significant improvement in skin quality, pruritus, hydration, pain, erythema,

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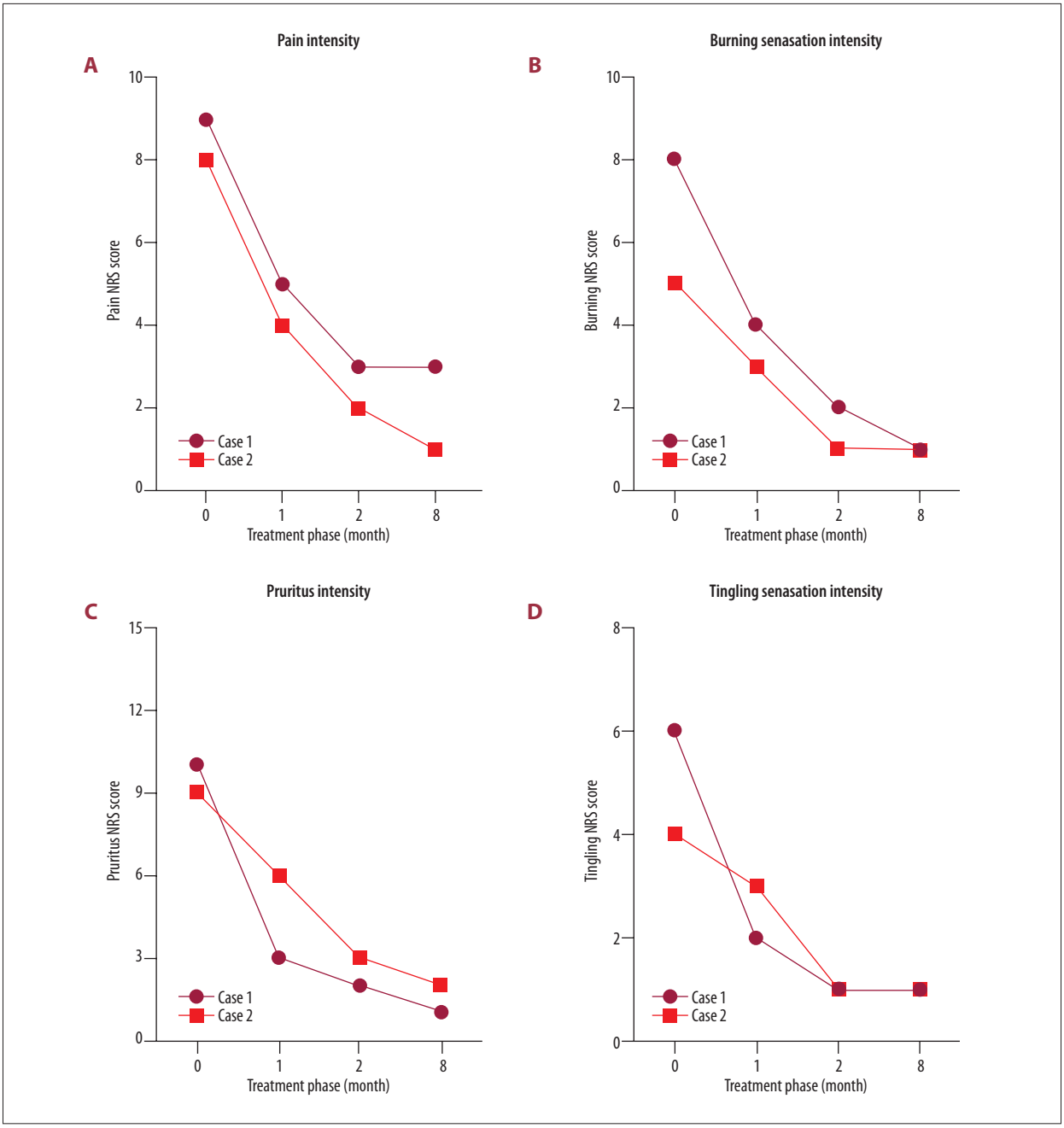

Figure 2. Changes in neurosensory symptoms during treatment with HMWNCHA and SA. Patient-reported symptom severity during treatment in Cases 1 and 2. Pain (**A**), burning sensation (**B**), pruritus (**C**), and tingling (**D**) were evaluated using the NRS, with 0 representing no symptoms and 10 representing the worst imaginable symptoms. Scores were recorded at baseline before treatment initiation, after the first treatment session, and after the second treatment session. Both patients demonstrated progressive improvement in all evaluated neurosensory symptoms throughout treatment. NRS, Numerical Rating Scale; HMWNCHA, high-molecular-weight non-crosslinked hyaluronic acid; SA, succinic acid.

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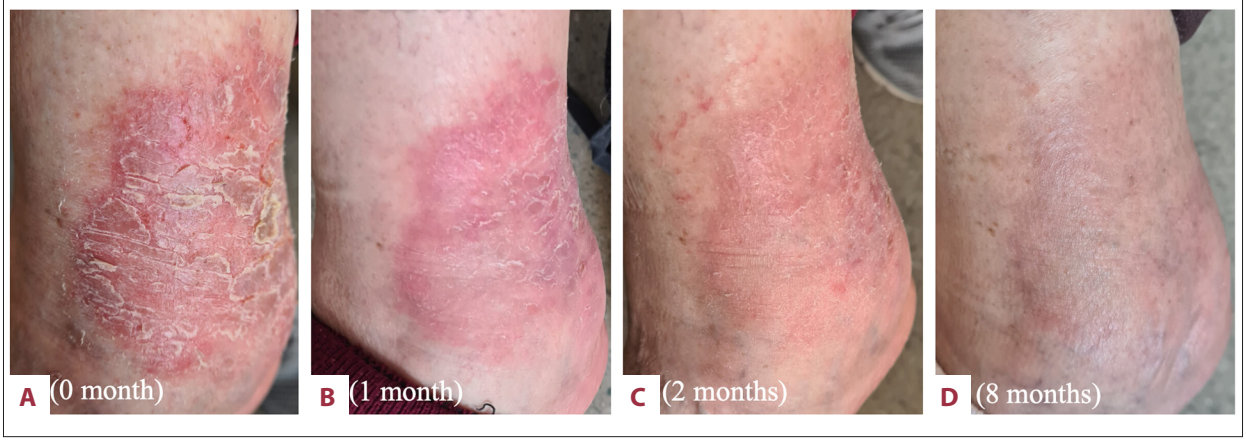

Figure 3. Clinical improvement of unilateral stasis dermatitis following intradermotherapy with HMWNCHA and SA in Case 2. Serial clinical photographs of a 75-year-old female patient with unilateral stasis dermatitis of the left ankle treated with intradermal microinjections of HMWNCHA combined with SA. (**A**) Baseline presentation showing an erythematous lesion associated with xerosis and skin damage. (**B**) Clinical appearance 1 month after the first treatment session, demonstrating reduction in erythema and improvement in skin hydration. (**C**) Clinical appearance 1 month after the second treatment session (2 months after treatment initiation), showing marked reduction in lesion size and progressive skin regeneration. (**D**) Six-month follow-up after the second treatment session (8 months after treatment initiation), demonstrating near-complete resolution of the lesion and maintenance of clinical remission. HMWNCHA, high-molecular-weight non-crosslinked hyaluronic acid; SA, succinic acid.

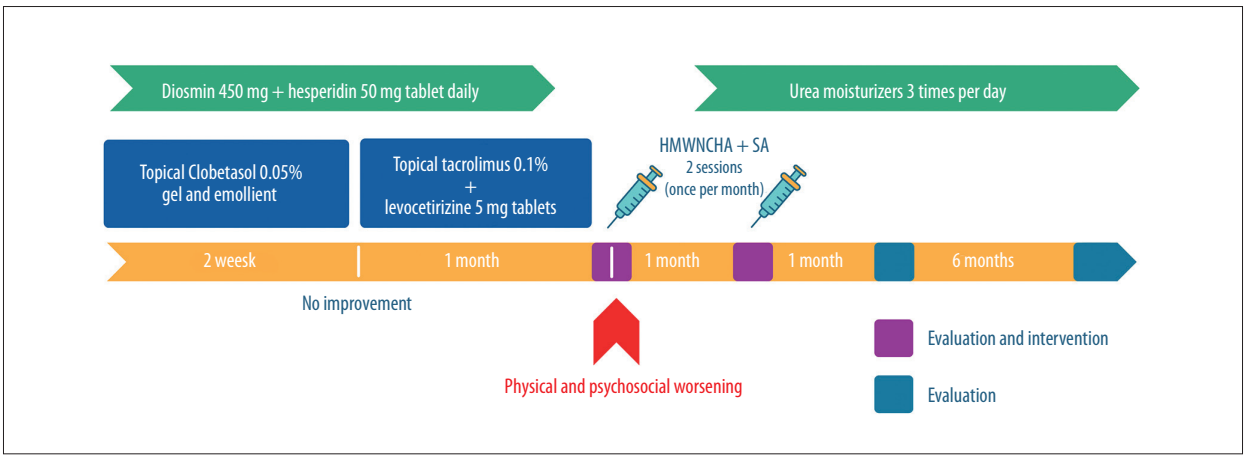

Figure 4. Timeline of clinical evaluation, treatment, and follow-up in the 2 patients with stasis dermatitis. Schematic representation of the clinical management in Cases 1 and 2. Both patients underwent baseline clinical evaluation following failure of conventional therapy, including topical corticosteroids, topical tacrolimus, oral antihistamines, compression therapy, and lifestyle measures. Intradermotherapy with HMWNCHA combined with SA was administered in 2 treatment sessions separated by 1 month. Clinical assessments of skin condition and symptom severity were performed at baseline and after each treatment session. Long-term follow-up was conducted 6 months after the second treatment session, demonstrating sustained clinical remission in both patients while receiving emollient therapy alone. HMWNCHA, high-molecular-weight non-crosslinked hyaluronic acid; SA, succinic acid.

and mobility was observed after the first session, with marked reduction in lesion size and near-complete skin regeneration after the second session (**Figures 2, 3**). At her 6-month follow-up, the patient remained in remission on emollient therapy alone, with no recurrence.

Both cases reported in this manuscript followed the treatment plan and evaluation summarized in **Figure 4**.

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Discussion

These 2 cases suggest that intradermal administration of HMWNCHA plus SA may be associated with improvements in patients of advanced age with refractory stasis dermatitis. The observations also highlight the potential importance of addressing both cutaneous and quality-of-life outcomes in the management of this challenging condition.

Stasis dermatitis is characterized by troublesome symptoms that substantially impair patients' quality of life. Emerging treatments, including pulsed light therapy, diode laser therapy, and platelet-rich plasma, have been proposed; however, these approaches are costly, supported by limited evidence, and predominantly studied in younger patient populations for whom sclerotherapy or surgery is feasible [15,16]. Published reports evaluating novel therapeutic approaches for stasis dermatitis remain scarce. Godoy et al described clinical improvement in a small case series treated with aminaphtone [17], while Nagai et al reported successful management of refractory stasis dermatitis using omega-3-acid ethyl esters [18]. However, in both cases, vascular surgeons declined surgical or sclerotherapy interventions due to patient age and healthcare coverage limitations. Moreover, patients of advanced age often exhibit a poorer therapeutic response and a more refractory or recurrent disease course, likely reflecting age-related alterations in skin barrier function, immune regulation, and sensory neural processing. Our previous study demonstrated that aging impairs both functional responsiveness and molecular signaling in sensory neurons, resulting in altered itch processing [19].

The diagnostic criteria for stasis dermatitis generally include involvement of the lower legs, underlying venous insufficiency, chronicity, bilateral symmetry, and cutaneous pigmentation changes. In the patient in Case 2, symmetry and pigmentation were absent; however, given the presence of venous insufficiency and characteristic ankle involvement, the condition was considered to represent an early-stage presentation of stasis dermatitis. In both patients, persistent pruritus was associated with sleep disturbance, impaired mobility, and psychological distress, highlighting the substantial psychosocial burden of refractory disease and the potential for a self-perpetuating itch-stress cycle. Notably, anhedonia has been recognized as an important component of psychological distress in patients with chronic itch and may further contribute to impaired quality of life.

Furthermore, psychological stress can exacerbate chronic inflammation through neuroendocrine pathways, contributing to disease persistence and impaired skin barrier function, and delayed healing [20,21]. This is particularly relevant in patients of advanced age, in whom psychosocial vulnerability and reduced resilience may amplify disease burden and negatively impact treatment outcomes.

The therapeutic effects observed in our cases may be explained by the complementary and potentially synergistic actions of HMWNCHA and SA. HMWNCHA exerts anti-inflammatory effects by downregulating pro-inflammatory cytokine production and promoting macrophage polarization toward an M2 reparative phenotype, while simultaneously supporting tissue regeneration through enhanced keratinocyte and fibroblast function, improved extracellular matrix organization, and restoration of skin hydration and barrier integrity [22,23]. SA contributes additional immunomodulatory effects, partly through activation of the succinate receptor SUCNR1, resulting in reduced expression of pro-inflammatory mediators such as TNF-αand IL-6 and further support of M2 macrophage polarization. SA has also been shown to enhance epithelial barrier function and tissue repair [24]. Although SA can exert pro-inflammatory effects under certain metabolic conditions, its controlled intradermal delivery in combination with HMWNCHA may favor a reparative microenvironment. Importantly, intradermal administration may allow targeted delivery to the dermal compartment, optimizing local bioavailability while minimizing systemic exposure, which could be particularly advantageous in patients of advanced age with multiple comorbidities [25]. In stasis dermatitis, a condition characterized by chronic inflammation, tissue hypoxia, impaired healing, and pruritus that leads to scratching that can result in secondary skin changes such as lichenification [26], HMWNCHA plus SA may contribute to symptom relief and restoration of skin integrity.

Conclusions

In these 2 septuagenarian patients with refractory stasis dermatitis, intradermal HMWNCHA plus SA was associated with marked clinical and psychosocial improvement. Although limited by the small number of cases, these findings support further investigation of this approach as a potential therapeutic option for refractory stasis dermatitis.

Acknowledgments

During the preparation of this work, the authors used ChatGPT (Open AI) solely for language polishing and grammatical refinement of non-scientific content. All critical scientific components, including research design, data analysis, and result interpretation, were exclusively conducted by human authors. The final manuscript has been thoroughly reviewed and approved by all coauthors who take full responsibility for its academic integrity and accuracy.

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Department and Institution Where Work Was Done

Centro de Especialidades Primarias San Lazaro, Santiago, Chile.

Informed Consent

Each subject signed a comprehensive written informed consent that included granting permission for the acquisition and publication of photographs.

The study was conducted in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. The presented intervention was approved by the director and ethical committee CEP Lazaro #052024.

Statement

The authors declare that the manufacturer had no role in the study design, data collection, data analysis, interpretation of results, figure preparation, or manuscript writing. Furthermore, no products were provided free of charge or at a discounted rate by the manufacturer, and the study was conducted independently without any form of industry involvement or influence.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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