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Case Report

Successful Treatment of Refractory Chronic Hand Eczema with Iontophoresis of Exosome from Adipose Tissue-Derived Mesenchymal Stem Cells

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Abstract

Chronic hand eczema (CHE) is a common dermatologic disease with a chronic and relapsing clinical course, and its treatment is challenging because the etiology is uncertain. Exosomes from adipose tissue-derived mesenchymal stem cells (ASC-exosomes) decrease the inflammatory response and repair the epidermal barrier. We report one case of refractory CHE treated successfully with iontophoresis of exosomes from human ASC. Further studies to establish the efficacy of exosomes from ASC in the treatment of CHE are promised. The patient experienced significant improvement after six treatment sessions, with resolution of itching and regression of lichenified plaques. No recurrence was observed during a 6-month follow-up period. ASC-exosomes demonstrated excellent tolerability without adverse effects. Iontophoresis enhanced transdermal delivery, supporting its potential as an effective administration method. This case suggests that ASC-exosomes may be a novel therapeutic option for patients with recalcitrant CHE.

Keywords: chronic hand eczema; mesenchymal stem cell; exosome

Introduction

Exosomes are nanovesicles (30-200nm) released by almost all cells and found in all body fluids [1]. Exosomes deliver their cargo (proteins, lipids, and nucleic acids) from originating cells to recipient cells, making them an appealing cell-free bio-materials to treat inflammatory diseases [2, 3]. Exosomes are recognized as the key component that regulates MSCs' paracrine effect [4]. A previous study showed that ASC-exosomes reduce atopic dermatitis symptoms in animal models by decreasing systemic inflammation [5]. ASC-exosomes improve epidermal permeability barrier functions by significant increase in ceramides and a reduction in immune responses [6]. Also, notably, ASC-exosomes delivered immediate clinical improvements in DFR, a result not typically seen with other treatment approaches [7]. These findings suggest that ASC-exosomes can be a promising treatment option for CHE, which is unresponsive to conventional modalities such as topical steroids. CHE is characterized by recurrent itching and painful erythematous papules and vesicles followed by lichenification, scaling, hyperkeratinizing, and skin fissuring. This condition is sometimes debilitating and refractory to treatment. We report one case of refractory CHE managed successfully with iontophoresis of ASC-exosomes.

Case Presentation

A 24-year-old male presented to our clinic with severe hand dermatitis. His past medical history was significant for seasonal allergic rhinitis and atopic dermatitis of childhood. Itchy, small erythematous plaques initially presented on dosal part of both hands, which had been developing for 3 years. Since then, the lesion had gradually spread and lichenified, and painful skin fissures had appeared. The patient had been treated with various steroid ointments, oral steroids, oral antihistamines, and emollients. However, the symptoms were slightly improved, and the patient was concerned about prolonged oral medication. On the physical examination, hyperkeratotic erythematous plaques with some scaling and fissuring were observed on the dorsum of both hands (Figure 1A). ASC-exosome were prepared, and 1.5mL of ASC-exosome solution (ExoCoBio Inc., Republic of Korea) was applied on each hand. For enhancing the delivery of ASC-exosome, we used an iontophoresis machine (Ionzyme) at 50mA. We treated the patient twice a week with 3 days interval. The itching subsided 1 week later, and lichenified plaque was regressed 3 weeks later (Fig.1B). No recurrence was detected at a subsequent 6-month follow-up examination.

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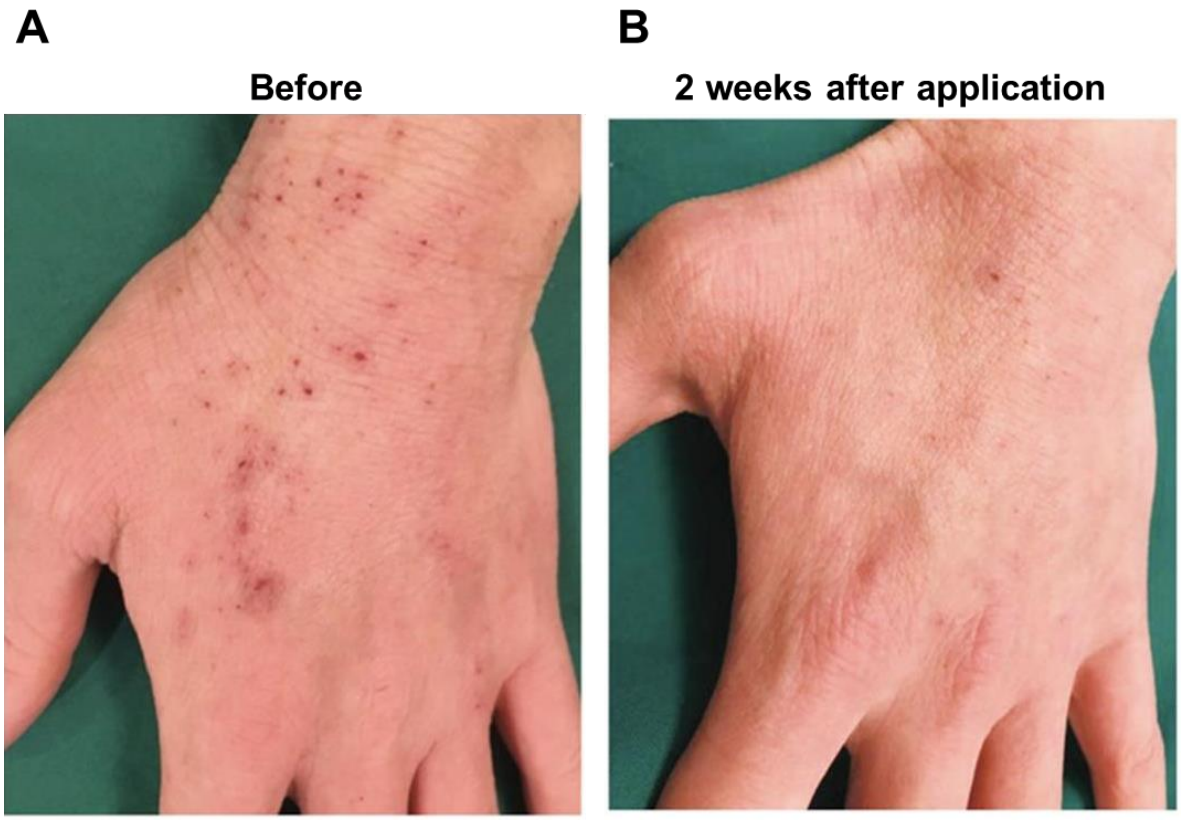

Figure 1: (A) The Image obtained before topical application of ASC-exosomes. Exosomes were applied to the entire face of the patient using iontophoresis. (B) The image was obtained 2 weeks after topical application of ASC-exosomes, which improved previous CHE in the patient.

Discussion

We report one case of refractory CHE which have been successfully managed with ASC-exosomes by using an iontophoretic device. CHE often impairs the quality of life but is frequently very recalcitrant. There are various treatment options, including topical corticosteroids or calcineurin inhibitors, phototherapy, systemic immune modulators, anti-psoriasis biologics, and in trader malbotulinum toxin [8-10]. However, these treatments are often associated with partial, unsatisfied response or tolerability. The preclinical trial of mesenchymal stem cell (MSC)-derived exosomes has been investigated in various disease models [11]. Several studies have shown that MSC-derived exosomes carry the essential properties of MSCs, suggesting that exosomes may be a compelling alternative to MSCs in regenerative and aesthetic medicine, as they would avoid most of the problems associated with live MSC-based therapy [12]. Interestingly, recent studies have shown that human adipose tissue stem cell-derived exosomes possess the critical properties of stem cells and are as potent as MSCs in the repair of various organ injuries [13, 14]. ASC-exosomes were found to reduce pathological symptoms of atopic dermatitis, such as clinical score, the levels of serum IgE, the number of eosinophils in blood, and the infiltration of mast cells in the animal model [5]. They also significantly reduced mRNA expression of inflammatory cytokines such as interleukin (IL)-4, IL-23, IL31, and tumor necrosis factor-a (TNF-a) in AD skin lesions of Nc/Nga mice [5]. In another animal study, ASC-exosomes promoted epidermal barrier repair by inducing de novo synthesis of ceramides and modulated the multiple gene expression program, including differentiation of keratinocytes, lipid metabolism, cell cycle, and immune response [6]. ACS-exosomes are nano-size particles, which are enough to penetrate damaged skin. They also have a negative charge. Iontophoretic transdermal delivery helps ASC-exosome to go through deep tissue and improve their therapeutic efficacy. In our hands, ASC-exosomes have proven useful in the management of one case with CHE. The patients in this case had no

intolerability and side effects during treatment. He was very satisfied with stopping oral medication and improving his quality of life. ASC-exosomes are a safe and effective choice for the treatment of refractory CHE. However, the present study had a limited sample of cases. Therefore, large sample randomized controlled trials supporting these results are required.

Conclusion

This case report highlights the successful treatment of chronic hand eczema (CHE) refractory to conventional therapies using iontophoretic delivery of ASC-exosomes. The patient experienced significant clinical improvement without adverse effects, indicating that ASC-exosomes, when combined with iontophoresis, may offer a novel, safe, and effective therapeutic approach for recalcitrant CHE. Given the encouraging outcome observed in this single case, further large-scale, controlled clinical studies are warranted to validate the therapeutic potential and establish standardized protocols for ASC-exosome based treatments in chronic inflammatory skin diseases.

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