RESEARCH ARTICLE OPEN ACCESS

Therapeutic Potential of Wharton's Jelly Mesenchymal Stem Cells-derived Secretome (S-MSCs) in Psoriasis Vulgaris: A Case Study

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Submission July 31, 2024
Accepted August 29, 2024
Available online on August 30, 2024

ABSTRACT

Background: Psoriasis is a chronic, immune-mediated skin disease that also has systemic manifestations. **Case:** In this report, we discuss our findings about a 47-years old psoriasis suffering male patient with a Psoriasis Area Severity Index (PASI) score of 10.8, treated with Wharton's Jelly Mesenchymal Stem Cells-derived Secretome (S-MSCs). Remarkably, complete regression was recorded within a treatment period of a week only. **Result:** The patient demonstrated a decrease in PASI, from 10.8 to 3.2 after 1 infusion and followed by 4 intramuscular injections of S-MSCs. Bioactive factors secreted by MSCs, cytokines and growth factors, are very likely to be the principal molecules which play a vital role in inflammatory modulation and skin tissue regeneration. No serious adverse events were noted for the patient as a result of secretome infusion and intramuscular injection. **Conclusion:** This report demonstrates safety and promises to be an effective strategy using S-MSCs treatment for managing the psoriatic issue and, thus, may offer as an alternative approach to overcome the limitations of the cell-based therapy.

Keyword : Psoriasis, MSCs, Secretome

INTRODUCTION

Psoriasis is a chronic autoimmune skin disorder characterized by keratinocytes hyperproliferation, leading to the formation of erythematous plaques with silvery scales [1–3]. Current available treatments frequently include topical medication, phototherapy, and systemic immunosuppressants, but these approaches may have limited efficacy and are associated with various adverse outcomes [1,4]. The recent statistic from Global Psoriasis Atlas have been reporting that over 60 million people are living with psoriasis in 19% of the world's countries [1.] Plaque psoriasis, also known as psoriasis vulgaris, is the most prevalent form of the disorder (about 90% of symptoms), and is distinguished by red patches with white scales on top [5]. Psoriasis vulgaris primarily affects the areas includes scalp, knees, elbows, hands, nails, and feet [6.]

T-helper cells play an essential part in psoriasis, an autoimmune-inflammatory disease that is potentially genetically predisposed [3,4]. Th cells have long been recognized as a crucial pathogenic element in psoriasis. In this condition, the majority of invading CD4+ T cells are Th1 cells, which primarily release pro-inflammatory cytokines including IFN-γ, IL-2, and IL-12 into affected dermal area. IFN-γ released by Th1 may trigger monocytes, dendritic cells (DCs), and endothelial cells activation in psoriasis patients [6,7]. In addition, IFN-γ may inhibit keratinocytes apoptosis, suggesting its role in inducing the keratinocytes hyperproliferation [6]. However, anti-IFN-γ chemical medication for controlling psoriasis has produced unfavorable results, implying that other molecular pathways are more intricately associated to the psoriasis pathogenesis. With the advances of research in the immunopathogenesis of psoriasis, a recent pathogenic model for psoriasis has demonstrated the relevance of the IL-23/Th17 immune axis [8]. Among the diverse molecules related to this axis, tumor necrosis factor (TNF)-α, IL-23, IL-17 and IL-22 have been established as the key regulators of psoriasis based on the profound effects of biologics targeting these molecules [9].

Recent breakthroughs in regenerative medicine have investigated the efficacy of MSCs and their secretory substance, secretome, in addressing inflammation-related conditions such as psoriasis [10–12]. MSCs are multipotent adult stem cells with a high proliferative ability while remaining undifferentiated [13–15]. The resulting daughter cells may differentiate into numerous types of cells found in the recipient tissue, assisting in the healing of tissue injury [16]. Due to their tissue regenerative and immunological modulatory properties, MSCs have the potential to serve as an effective agent in cell-based therapy [17]. MSCs' capabilities have captured the interest of scientists and doctors, who are seeking insight into the mechanisms underlying their curative and tissue regeneration abilities. MSCs isolated from Warton's Jelly tissue have received attention for their immunomodulatory properties and release of bioactive substances that may regulate immune responses and enhance tissue healing [18].

CASE REPORT

Patient

We discuss the case of a 47-year-old Indonesian male patient who was diagnosed with moderate psoriasis vulgaris that did not receive standard treatment. The patient had large plaque lesions that covered almost 20% of his body surface area, which had a negative influence on his quality of life. The disease's severity was determined to be 10.8 on the PASI, which is computed using the conventional approach that includes severity (erythema, induration, and desquamation) and percentage of affected area. After gaining informed consent, the patient was treated with S-MSCs. Under sterile environments, the S-MSCs was formulated and delivered as intramuscular injections into specific plaque lesions.

Preparation of Secretome-WJ-MSCs

S-MSCs was obtained from WJ-MSCs conditioned media at passage 8. After being centrifuged at 13000 xg for 10 min at 4°C, the conditioned medium (CM) of WJ-MSCs was filtrated from the culture condition. To isolate S-MSCs, tangential flow filtration (TFF) was used (Formulatrix, MA, USA) with several molecular weight cut-off categories in our previous studies. 2-1000 kDa filter cassettes separated the CM molecules. S-MSCs was then kept at -20°C before being used for subsequent experiments.

Treatment Protocol

The treatment protocol involved 2 cc S-MSCs infusion and followed by daily intramuscular injections of 1,3 cc S-MSCs for 4 days. Each injection targeted active psoriatic lesions identified by clinical assessment. The patient also topically administrated S-MSCs gel every day in affected area. The patient was monitored closely for any adverse effects throughout the treatment period. The patient did not take any other medication during the follow up period of 7 days and led an improved quality of life without any adverse events.

RESULT

Clinical Outcomes

On the day of first infusion, the PASI score of the patient was 10.8 (Fig. 1A, 2A, 2B), with thick silvery scales and erythema in interphalangeal joints and lower limbs. Within a week of initiating treatment, the PASI score was 3.2 (Fig. 1B, 2C, 2D), the patient demonstrated noticeable improvement in psoriatic lesions, characterized by reduced erythema, scaling, and induration. By the end of the 7-days treatment course, nearly 60% clearance of psoriatic plaques was observed, accompanied by a marked improvement in overall skin texture. Both infusion and intramuscular injection procedure were well tolerated, with no evidence of adverse reactions being recorded throughout 1 week monitoring.

Follow-up and Maintenance

Following the completion of treatment, the patient was followed up every day until 7 days post treatment to assess the sustainability of therapeutic response and to monitor for any recurrence of psoriatic lesions. Maintenance therapy with topical emollients and periodic evaluations were recommended to optimize long-term outcomes.

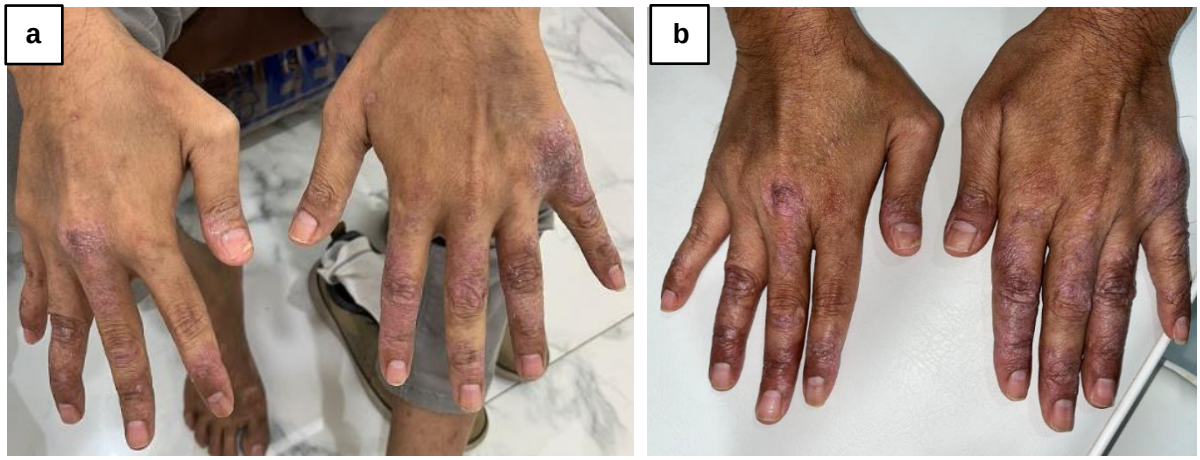

Figure 1. Effect of S-MSCs on psoriasis vulgaris. The interphalangeal joints of patient before S-MSCs treatment (a). Regression of psoriasis and a complete clearance of inflammatory erythematous plaques recorded after infusion, intramuscular injection and topical application of S-MSCs for a period of a week (b).

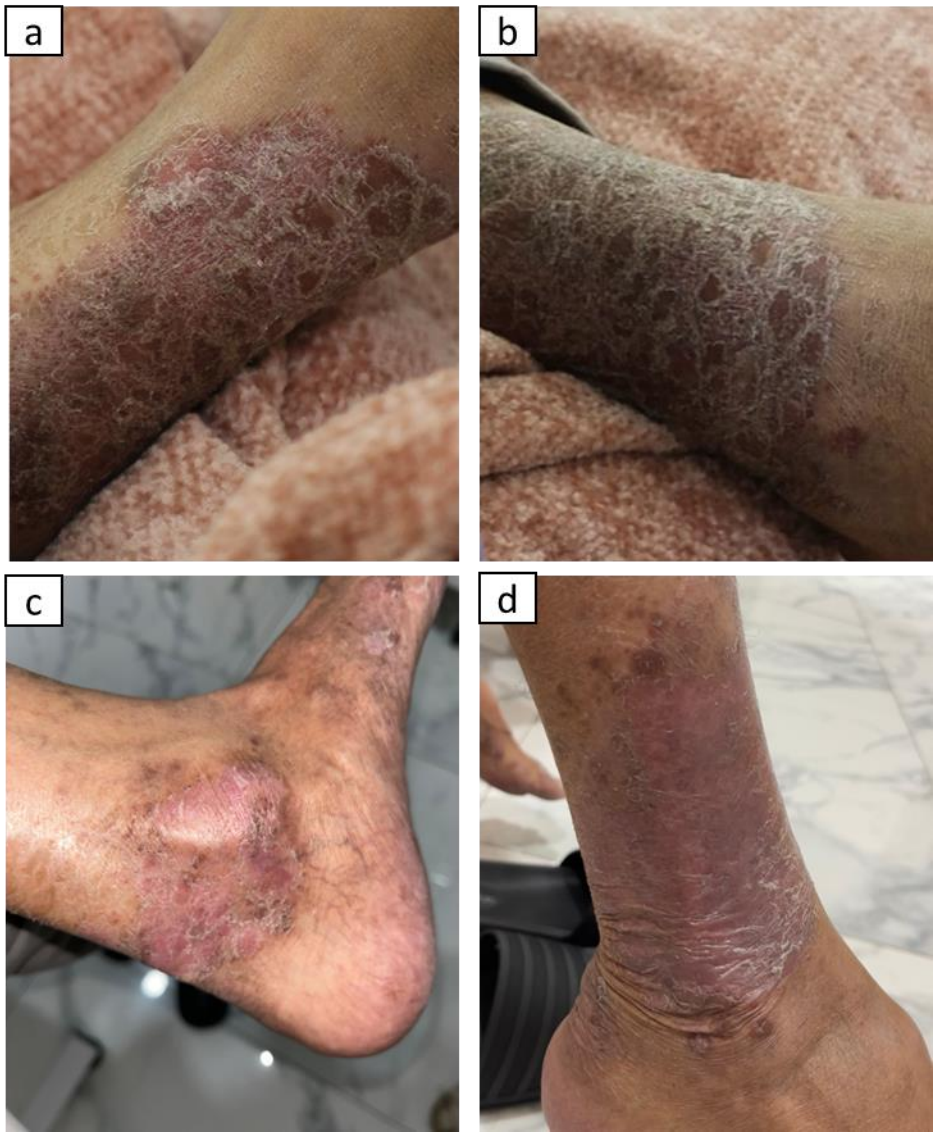

Figure 2. Effect of S-MSCs on psoriasis vulgaris. The lower limbs of patient showing numerous erythematous plaques with adherent silvery flakes before S-MSCs treatment (a, b). Regression of psoriasis and a complete clearance of inflammatory erythematous plaques recorded after infusion, intramuscular injection and topical application of S-MSCs for a period of a week (c, d).

DISCUSSION

This case report highlights the promising role of S-MSCs in the management of moderate psoriasis vulgaris. Psoriasis is a chronic inflammatory skin disease with a diverse range of clinical symptoms. Its skin manifestations include the hyperproliferation of basal keratinocytes, a thickened, scaly epidermis, and the infiltration of inflammatory cells into the skin [19]. Conventional treatments include topical corticosteroids, systemic immunosuppressants, and biologic therapies targeting specific cytokines involved in the inflammatory cascade [20]. However, these treatments may not be effective for all patients and can have adverse effects, necessitating exploration of alternative therapies. Therapies utilizing multipotent MSCs have demonstrated effectiveness in

treating psoriasis and similar skin conditions [21,22]. The clinical benefits observed may stem from the engraftment of MSCs or their paracrine and immunomodulatory effects. However, transplanting MSCs presents certain challenges, such as low cell survivability in the host due to a harsh microenvironment and significant cell loss resulting from inadequate or absent cell adhesion [23]. Emerging evidence suggests that the secretome of MSCs may have therapeutic potential in alleviating scalp psoriasis. This is supported by studies indicating that the bioactive molecules released by MSCs can modulate immune responses and promote tissue repair, leading to a reduction in the inflammation and hyperproliferation characteristic of psoriatic lesions on the scalp [23,24]. The clinical improvements observed indicate that bioactive factors released by WJ-MSCs may have strong anti-inflammatory and tissue-regenerative effects in psoriatic skin. These results imply that the MSCs secretome could be a promising treatment for psoriasis. However, further research is necessary to elucidate its mechanisms and refine its therapeutic application.

In this study, the treatment protocol involved infusion followed by daily intramuscular injections and topical administration of S-MSCs in patient with active psoriatic lesions. The decision to target lesions with intramuscular injections aimed to deliver the therapeutic agents directly to affected areas, enhancing local efficacy while minimizing systemic exposure [25]. The use of S-MSCs offers a novel approach by harnessing the paracrine signaling factors produced by stem cells [26]. These factors include anti-inflammatory cytokines, growth factors, and extracellular vesicles that modulate the immune response and promote tissue repair [26]. The topical gel formulation further facilitated sustained release and penetration of active components into the skin layers, optimizing therapeutic outcomes.

During the 7-day treatment period, the clinical results were encouraging. Patients exhibited significant improvement in psoriatic lesions, evidenced by decreased erythema, scaling, and thickness. Nearly 60% reduction in psoriatic plaques highlights the potential effectiveness of S-MSCs in alleviating psoriasis symptoms. Additionally, the noticeable enhancement in overall skin condition indicates a comprehensive therapeutic benefit that extends beyond lesion reduction, contributing to better quality of life for the patients.

The absence of adverse effects during the treatment and follow-up period is noteworthy, highlighting the safety profile of S-MSCs in this context. This finding is particularly significant given the potential risks associated with conventional systemic therapies for psoriasis. While these preliminary findings are encouraging, further studies involving larger patient cohorts and longer follow-up periods are warranted to validate the efficacy and safety of S-MSCs in treating psoriasis. Future research should also explore the underlying mechanisms of action and optimize treatment protocols to validate these findings and elucidate the underlying mechanisms of action.

CONCLUSION

In conclusion, S-MSCs represents a novel therapeutic approach for patients with refractory psoriasis vulgaris. This case report provides preliminary evidence supporting the efficacy and safety of S-MSCs in achieving significant clinical improvement and enhancing quality of life in psoriasis patients. The long-term effects of the treatment represent a limitation of this study, highlighting the need for follow-up research to fully understand the therapy's impact over time. Continued research in this field holds promise for the development of innovative biologic therapy for inflammatory skin disorders.

ACKNOWLEDGEMENT

We would like to express our sincere gratitude to the Stem Cell and Cancer Research (SCCR) Laboratory in Semarang, Indonesia, for their invaluable support and to everyone who contributed to this research.

FUNDING

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONTRIBUTORS

SYA and SP developed the study's concept and design. SYA and RA carried out the experiments, while SP was responsible for the data analysis. SYA wrote and revised the manuscript, with SP also providing feedback during the review process.

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