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Cellular and Extracellular Vesicle-Based Regeneration in Focal Vitiligo: A Novel Approach Using Adipose-Derived MSCs and Exosomes

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Abstract: ***Vitiligo is an acquired autoimmune pigmentary disorder characterized by progressive melanocyte loss, resulting in sharply demarcated depigmented macules. Conventional treatments often yield incomplete or temporary improvement, especially in long-standing cases. Recent advances in regenerative medicine have highlighted the therapeutic potential of mesenchymal stem cells (MSCs) and exosomes in restoring melanocyte function. We report the case of a 48-year-old male with focal vitiligo involving stable depigmented patches on both hands and legs for over two years, treated using a combined intravenous (IV) and intradermal (ID) protocol of donor-derived adipose MSCs and amniotic fluid–derived exosomes. This dual approach was designed to achieve systemic immune modulation alongside localized melanocyte stimulation. Across four treatment sessions, visible perifollicular repigmentation appeared within two weeks, progressing to nearly 90% pigment restoration by three months. No new lesions or adverse events were observed. This case supports the synergistic immunomodulatory and melanocyte-regenerative potential of MSCs and exosomes as an emerging modality for focal vitiligo.***

Keywords: Vitiligo; Focal vitiligo; Mesenchymal stem cells; Exosomes; Adipose-derived MSCs; Repigmentation; Immunomodulation; Regenerative therapy

1. Introduction

Vitiligo is a long-standing, acquired pigmentary disorder affecting 0.5–2% of the global population [1]. It results from immune-mediated melanocyte destruction, producing well-defined areas of depigmentation. Focal vitiligo, a localized subtype with one or a few isolated patches confined to a limited anatomical region, is often stable yet can significantly affect psychosocial well-being.

Melanocyte loss is driven by interacting genetic, oxidative, and immune-mediated mechanisms [2,7,12]. Cytotoxic T lymphocytes and inflammatory mediators—including TNF-α, IFN-γ, and IL-17—promote melanocyte apoptosis and disrupt melanogenesis [2,8]. Conventional treatments such as topical corticosteroids, calcineurin inhibitors, phototherapy, and surgical grafting frequently yield incomplete or transient repigmentation, with a high relapse rate.

Advances in regenerative medicine underscore the therapeutic potential of mesenchymal stem cells (MSCs) and their extracellular vesicles, particularly exosomes [3–5,9]. Adipose-derived MSCs secrete bioactive molecules—including anti-inflammatory cytokines, growth factors, and regulatory microRNAs—that enhance melanocyte survival, migration, and proliferation while restoring the dermal microenvironment. Through these paracrine actions, MSCs and exosomes concurrently modulate autoimmune activity and promote melanocyte regeneration.

We report a case of chronic focal vitiligo demonstrating rapid and sustained repigmentation following combined intravenous and intradermal administration of adipose-derived MSCs and amniotic-fluid–derived exosomes.

2. Case Presentation

A 48-year-old male presented with focal vitiligo, showing a few well-defined depigmented macules scattered over both hands and legs, persisting for approximately two years. The lesions were stable with no recent enlargement. The patient had a known history of autoimmune condition and previously had minimal response to topical corticosteroids and phototherapy. No family history of vitiligo or autoimmune disorders was reported.

After thorough clinical evaluation, the patient was enrolled for regenerative treatment using donor-derived adipose tissue MSCs and amniotic fluid–derived exosomes, identical to the combination used in our liver cirrhosis treatment protocol. The chosen MSC and exosome doses were based on prior internal clinical experience and published regenerative dermatology protocols. Informed consent was obtained.

Patient data

Parameter	Value
Age	48
Duration	2 years
Type	Focal vitiligo
Previous treatments	Steroid + phototherapy
Autoimmune history	Yes
Response	90% repigmentation

Treatment Protocol

- Stem cells: 200 million (2×10^8 cells) viable adipose-derived MSCs in four sessions
- Exosomes: ~90 billion (9×10^{10} particles) amniotic fluid–

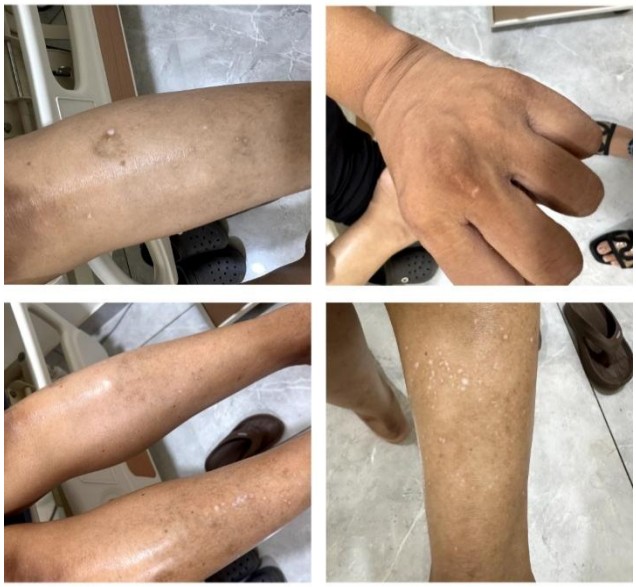
derived exosomes (TFF) in four sessions
- Route: Combined intravenous (IV-30mL) and intradermal (ID-01mL per lesion) administration
- Sessions: Four treatment sessions conducted over a period of three month

The MSCs were expanded under GMP and ISO-certified laboratory conditions, while exosomes were purified using tangential flow filtration (TFF) to ensure clinical-grade quality. Particle size was confirmed between ~80-150 nm. IV administration was selected for systemic immune modulation, while intradermal injections targeted melanocyte reservoirs directly. This dual approach maximizes the regenerative and immunomodulatory benefits of MSCs and exosomes.

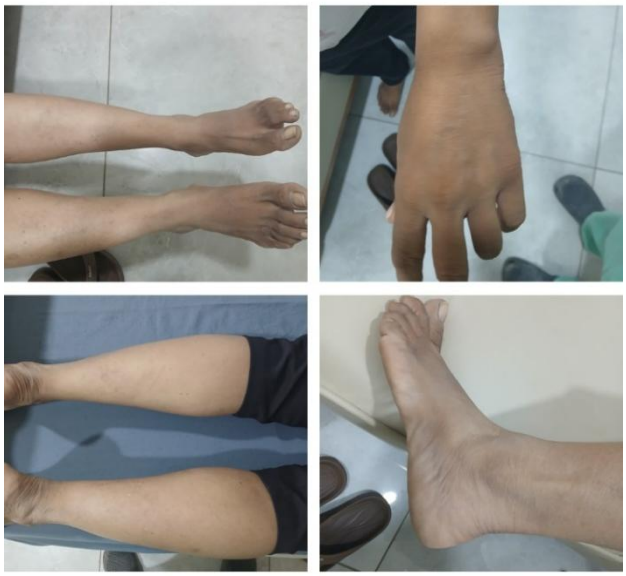
The therapy was well tolerated, and no adverse reactions, infections, or inflammatory flares were observed during or after treatment.

Clinical Progression
- **Baseline (Pre-treatment):** Multiple small, stable depigmented patches over both hands and legs consistent with focal vitiligo; no spontaneous repigmentation.
- **2 weeks post-treatment:** Visible perifollicular repigmentation began, particularly on lower legs and dorsal hands.
- **1 month:** Marked pigment expansion with >50% improvement noted; patient reported improved skin tone uniformity and confidence.
- **3 months (Follow-up):** Approximately 90% repigmentation achieved, with almost complete restoration of normal skin color and texture. No new lesions developed, and the existing areas remained stable.

Patient-reported outcome:
"After years of unsuccessful treatments, I finally saw color returning to my skin. Within a few weeks, I could see visible changes—Thanks to CELLSTAR & team, it's truly life-changing"



(a)



(b)

Figure 1: Baseline and 3-month post-treatment comparison. (a) Depigmented macules prior to therapy (b) Significant repigmentation after MSC + exosome therapy

3. Discussion

The encouraging clinical outcome in this patient underscores the complementary regenerative and immunoregulatory properties of MSCs and exosomes in autoimmune pigmentary disorders such as vitiligo [3, 4, 9, 10]. The combination of MSCs and amniotic fluid derived exosomes was selected to provide both systemic immune modulation and localized melanocyte-regenerative signaling, addressing key pathomechanisms of vitiligo including T-cell–mediated melanocyte injury, oxidative stress, and microenvironmental imbalance. The observed effect is likely the result of several concurrent biological mechanisms:

3.1 Immunomodulation

MSCs attenuate autoreactive T-cell activity and promote a regulatory T-cell phenotype through soluble mediators including IL-10, TGF-β, and PGE_2 [10, 11, 14]. This immune shift limits melanocyte-targeted cytotoxicity and helps re-establish local tolerance.

3.2 Melanocyte Regeneration

Exosomal cargo contains melanogenic factors such as bFGF, HGF, and SCF that encourage melanocyte proliferation and migration from follicular reservoirs into depigmented epidermis [4, 5, 10]. This regenerative stimulus accounts for the early perifollicular pigmentation seen after therapy.

3.3 Microenvironment Repair

By counteracting oxidative stress, diminishing local inflammation, and enhancing vascular remodeling, MSCs and exosomes recreate a supportive niche essential for melanocyte survival and pigment synthesis.

3.4 Paracrine Signaling

Specific exosomal microRNAs, notably miR-211 and miR-146a, regulate melanogenesis and immune-signaling cascades in vitiligo lesions, reinforcing pigment recovery.

Earlier investigations demonstrated that MSC-derived exosomes can suppress reactive oxygen species and reduce expression of CXCL10 and IFN-γ—key drivers of vitiligo pathogenesis [7, 11, 12]. In this case, combining systemic and intradermal delivery likely produced both immune stabilization and direct melanocyte stimulation, explaining the swift and sustained repigmentation.

Earlier studies have reported partial repigmentation with standalone cellular therapies; however, combining MSCs with exosomes may produce more rapid and durable outcomes due to synergistic paracrine activity. No recurrence or new lesions were noted during follow-up, indicating persistent immune balance. The absence of adverse effects further supports the safety of this hybrid cell-based and cell-free approach [14, 15].

4. Conclusion

This case demonstrates that combined intravenous and intradermal administration of donor-derived adipose MSCs and amniotic fluid–derived exosomes can achieve significant repigmentation in chronic focal vitiligo. The patient achieved approximately 90% repigmentation within three months without recurrence or adverse events. The patient was monitored for three months post-treatment, during which no new lesions or relapse were observed. These findings are consistent with previous regenerative dermatology studies [9,14,15].

The observed clinical success reinforces the concept that regenerative cell–based therapies may restore melanocyte function and immune homeostasis in vitiligo, offering a promising alternative to conventional therapies. This case supports further controlled investigations to determine optimal dosing, delivery routes, and long-term safety. Long-term follow-up studies will be essential to determine durability of repigmentation.

5. Limitations

Being a single-patient case report, generalizability is limited. Long-term follow-up and controlled clinical studies are required to validate these findings. Future studies involving larger cohorts and standardized dosing protocols are needed.

Conflicts of Interest
The authors declare no conflicts of interest. Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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Ethical Statement
Ethical approval was not required for this single case report; however, all procedures were performed in accordance with institutional guidelines.

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