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Case report

Treatment of persistent chemotherapy-induced hair loss (Alopecia) with human mesenchymal stromal cells exosome enriched extracellular vesicles: A case report

Amir Hossein Norooznezhad [a], Reza Yarani [a], Mehrdad Payandeh [a,b], Zohreh Hoseinkhani [a], Hamidreza Mahmoudi [c], Sarah Kiani [a], Kamran Mansouri [a,*,1]

[a] Medical Biology Research Center, Health Technology Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran
[b] Bone Marrow Transplantation Department, School of Medicine, Kermanshah, University of Medical Sciences, Kermanshah, Iran
[c] Autoimmune Bullous Diseases Research Center, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Introduction: Cancer is among the leading causes of death worldwide and affects a considerable number of individuals. Chemotherapy is one the most common treatment for this condition and hair loss is among one of the most prevalent side effects. In this study, we report successful treatment of a patient suffering from persistent chemotherapy-induced alopecia (PCIA) with extracellular enriched vesicles (EVs) derived from human placental mesenchymal stromal cells (MSCs).

Case presentation: The patient was a 36-year-old woman with a history of invasive ductal carcinoma, underwent six courses of chemotherapy with paclitaxel and adriamycin. Following this treatment and for almost 18 months, she, unfortunately, had no regrowth of hair except some light vellus hairs on the scalp. She then received MSC-derived EVs with scalp injection (subcutaneous) every 4 weeks for 3 continuous months at which point she presented complete regrowth of terminal hair on her scalp.

Conclusion: This report demonstrates that MSC-derived EVs could be a possible treatment for permanent chemotherapy-induced alopecia; however, further studies and trials are necessary.

1. Introduction

Chemotherapy-induced hair loss usually occurs in more than half of cases undergoing this treatment which causes emotional trauma to patients. According to studies, approximately 47% of women who undergo chemotherapy reported hair loss as their biggest traumatic stress during treatment [1].

During the past few decades, human mesenchymal stromal cells (MSCs) have been used in the clinic with no significant reported side effects [2]. In addition to the parent cells, studies have used the extracellular enriched vesicles (EVs), especially exosomes secreted by MSCs, as a cell-free treatment for a wide range of diseases [3,4]. These extracellular vesicles, which contain lipids, proteins, and

* Corresponding author.
E-mail addresses: kmansouri@kums.ac.ir, kamranmansouri@gmail.com (K. Mansouri).
[1] Postal address: Medical Biology Research Center, Health technology Institute, School of Medicine, Kermanshah, University of Medical Sciences, Kermanshah, P.O. Box 67145-1673, Iran.

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nucleic acids, represent their origin or parent cell. Due to their immunomodulatory properties and regenerative abilities, these EVs have therefore been considered potential treatments for many diseases in the field of dermatology [5]. Moreover, it has been shown that dermal papilla mesenchymal stem cell exosomes were able to induce development of hair follicles in an *in vitro* model as well as hair growth in *in vivo* models [6].

This study reports the successful treatment of a 36-year-old woman with chronic persistent chemotherapy-induced alopecia (PCIA) using human placental MSC-derived extracellular enriched vesicles.

2. Case presentation

A 36-year-old woman with a history of invasive ductal carcinoma in the left breast was referred to our center complaining of post-chemotherapy hair loss followed by insufficient hair regrowth after the end of treatment despite waiting for 18 months. Following a left breast lumpectomy and axillary lymph node dissection, she underwent six courses of chemotherapy with paclitaxel and adriamycin (every three weeks) as well as radiotherapy sessions. At the time of her visit, she was receiving tamoxifen and supplemental tablets containing vitamins B family, C, and D, zinc, selenium. The patient was otherwise healthy and had no significant medical or family history. She reported complete hair loss during chemotherapy followed by insufficient hair regrowth after the end of treatment. The patient had tried many different treatments such as platelet-rich plasma (PRP) therapy, mesotherapy, and different oral (e.g., zinc, selenium, and herbal supplements)/topical (minoxidil) medications which none of them had no effect on the hair re-growth. On examination, the patient had complete hair loss in the scalp except for some light vellus hairs (Fig. 1; 1.1–1.4). Otherwise, the skin examination was normal. All laboratory investigations were normal, including a complete blood count, serum ferritin, iron, total iron-binding protein, and hormonal and endocrine assessments. No other previous treatment with stem cells has been conducted for the PCIA.

Considering the already mentioned condition, the patient candidate for treatment with allogenic human MSC-derived EVs for three sessions (140–160 μg; 2.5–3.2 $\times$ 10^{10} particles every four weeks). As described previously by our team, human mesenchymal stem/stromal cells were isolated from the human placenta and the EVs were purified [7]. The suspension was injected subcutaneously into 12 equally distributed areas of the scalp for three times with interval of each two months. Following the intervention, no adverse effect such as fever, chills, fainting, nausea, vomiting and skin reactions was not observed. After three months, there was a complete regrowth of terminal hair on the scalp (Fig. 1; 2.1–2.4). She was followed for ten months and demonstrated hair growth up to 8–9 cm and no adverse event was observed. This study was approved by Medical Ethics Committee of Kermanshah University of Medical Sciences, Kermanshah, Iran by IRIB number of IR.KUMS.MED.REC.1401.211.

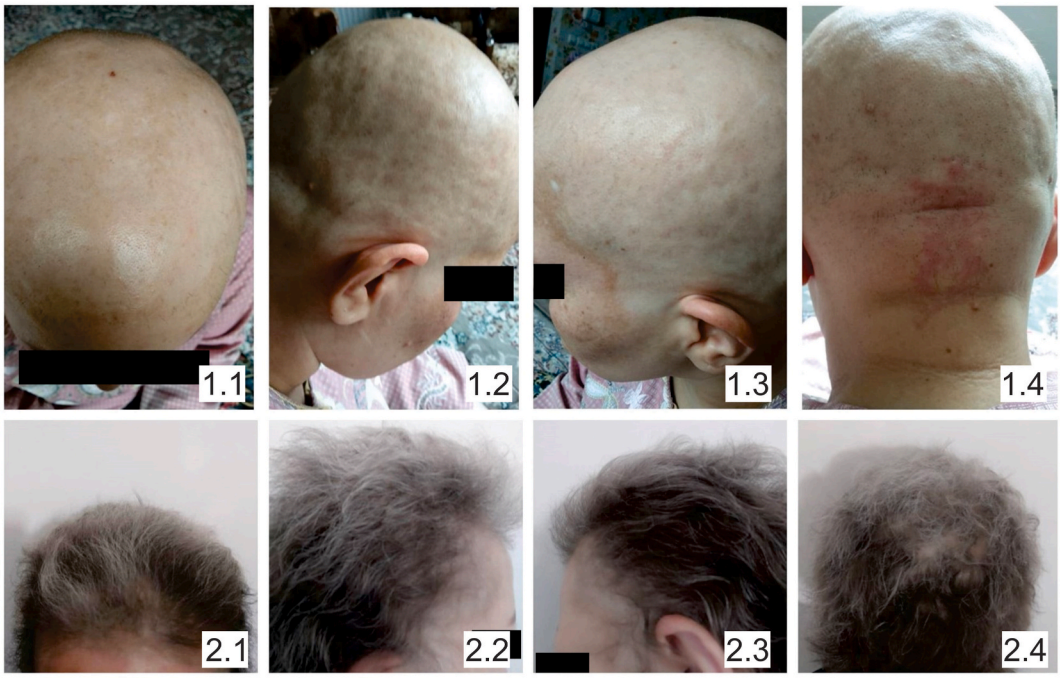

Fig. 1. Treatment of persistent chemotherapy-induced hair loss (alopecia) with human mesenchymal stromal cells extracellular enriched vesicles. (Lower line: Pre-treatment and upper line: 8 months after the treatment).

3. Discussion

In this study, human MSC-derived extracellular EVs were investigated as a treatment for PCIA in a patient with a history of breast cancer. The patient underwent three treatment sessions, and, as previously stated, the results were clinically promising and satisfactory for both the patient and the treatment team.

As a result of chemotherapy, any proliferating cells could be affected, including dividing cells in the hair matrix resulting in alopecia. PCIA has been reported since 1991 [8] and is defined as hair re-growth of <50% of the prechemotherapy amount of hair. It is still unclear what causes permanent alopecia following chemotherapy. Histologically, PCIA is mainly similar to androgenetic alopecia (AGA) in terms of preserved follicular units, increased vellus-like hairs, and increased follicular stelae. Nonetheless, an increase in telogen follicles has been observed, which is different from AGA. In light of the similarities between the two conditions, chemotherapy may cause AGA in individuals predisposed to the condition. However, the clinical features are mostly different with AGA. One more probable hypothesis is that PCIA may result from a substantial reduction in stem cells in the bulge or papilla. Despite its disappointing results in terms of quality of life for patients, because of its unclear pathophysiology, there is still no treatment for PCIA [9].

Interestingly, Rajendran et al. published a study assessing the effect of treatment with human extracellular vesicles on proliferation and migration of dermal papilla, as well as the release factors from this source. It has been demonstrated that extracellular vesicles increased dermal papilla proliferation and migration. Moreover, this treatment was able to increase the levels of phosphorylated ERK and Akt and Bcl-2. Furthermore, following treatment with extracellular vesicles, vascular endothelial growth factor and insulin-like growth factor increased. The intradermal application of MSCEVs was effective in transforming mice from telogen to anagen [10]. The significant effect of extracellular vesicles on dermal papilla proliferation and migration and the upregulation of growth factor pathways are a few possible mechanisms behind its effectiveness in the treatment of PCIA. According to our knowledge, this study is the first to investigate the potential of human MSC-derived EVs as a therapeutic agent for PCAI. In addition, herein, we evaluate a single case involving placenta-derived extracellular enriched vesicles.

4. Conclusion

The current study showed the effeteness of treatment of PCIA with human mesenchymal stromal/stem cell-derived EV in one case. Further research involving a more significant number of patients and different MSC sources such as fat and placenta will shed more light on the efficacy of MSCs in PCIA.

Ethical statement

The patient freely signed a consent form letting the authors publish her data and images.

Author contribution statement

All authors listed have significantly contributed to the investigation, development and writing of this article.

Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no conflict of interest.

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Authors are grateful for kind cooperation of the patient in this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e15165.

References

[1] R.M. Trüeb, Chemotherapy-induced hair loss, Skin, Therapy. Lett. 15 (7) (2010) 5–7.
[2] M. Thompson, et al., Cell therapy with intravascular administration of mesenchymal stromal cells continues to appear safe: an updated systematic review and meta-analysis, EClinicalMedicine 19 (2020), 100249.

[3] V. Sengupta, S. Sengupta, A. Lazo, P. Woods, A. Nolan, N. Bremer, Exosomes derived from bone marrow mesenchymal stem cells as treatment for severe COVID-19, Stem Cell. Dev. 29 (12) (2020) 747–754.
[4] S.J.O. Tan, J.F. Floriano, L. Nicastro, C. Emanueli, F. Catapano, Novel applications of mesenchymal stem cell-derived exosomes for myocardial infarction therapeutics, Biomolecules 10 (5) (2020) 707.
[5] D.H. Ha, et al., Mesenchymal stem/stromal cell-derived exosomes for immunomodulatory therapeutics and skin regeneration, Cells 9 (5) (2020) 1157.
[6] M.I. Quiñones-Vico, et al., The role of exosomes derived from mesenchymal stromal cells in dermatology, Front. Cell Dev. Biol. 9 (2021), 647012.
[7] A.H. Norooznezhad, et al., Human placental mesenchymal stromal cell-derived exosome-enriched extracellular vesicles for chronic cutaneous graft-versus-host disease: a case report, J. Cell Mol. Med. 26 (2) (2022) 588–592.
[8] B.W. Baker, et al., Busulphan/cyclophosphamide conditioning for bone marrow transplantation may lead to failure of hair regrowth, Bone Marrow Transplant. 7 (1991) 43–47.
[9] M. Miteva, C. Misciali, P.A. Fanti, C. Vincenzi, P. Romanelli, A. Tosti, Permanent alopecia after systemic chemotherapy: a clinicopathological study of 10 cases, Am. J. Dermatopathol. 33 (4) (2011) 345–350.
[10] R.L. Rajendran, et al., Extracellular vesicles derived from MSCs activates dermal papilla cell in vitro and promotes hair follicle conversion from telogen to anagen in mice, Sci. Rep. 7 (2017), 15560.