BRIEF REPORT

Follicular microenvironment-targeted regenerative strategy in androgenetic alopecia: A preliminary case series combining autologous adipose micrografts and polynucleotides

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ABSTRACT

Background: Androgenetic alopecia (AGA) is a chronic multifactorial condition characterized by progressive follicular miniaturization. Beyond androgen-mediated mechanisms, increasing evidence highlights the role of perifollicular microinflammation, vascular alterations, and stromal remodeling in disease progression. Targeting the follicular microenvironment may therefore represent a complementary therapeutic strategy.

Objective: To evaluate the clinical and trichoscopic outcomes of a combined regenerative protocol based on autologous adipose-derived micrografting and intradermal polynucleotide administration in patients with AGA.

Methods: Four patients (two males and two females) with clinically and trichoscopically confirmed AGA were included. Disease severity was classified using the Norwood–Hamilton scale (male patients) and the Ludwig scale (female patients). All patients underwent a single session of autologous adipose-derived micrografting performed using a mechanical processing system (SEFFIHAIR®, SEFFILINE S.r.l., Bologna, Italy), combined with intradermal injections of polynucleotides (Nucleofill® Medium, Promoitalia S.r.l., Milan, Italy), followed by five additional polynucleotide sessions at two-week intervals. Clinical and trichoscopic assessments were conducted at baseline and at 4 months.

Results: Patients with early to intermediate AGA demonstrated reduced hair shaft diameter variability and improved apparent density. The advanced-stage patient showed mild qualitative improvement without significant density increase. No adverse events were observed.

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Conclusion: These preliminary findings suggest that the modulation of the follicular microenvironment through combined regenerative strategies may represent a potential adjunctive approach, particularly in early-stage AGA.

Key words: Androgenetic alopecia, Follicular microenvironment, Adipose-derived micrografts; Polynucleotides, Regenerative medicine, Trichoscopy

Introduction

Androgenetic alopecia (AGA) is the most common form of hair loss[1], characterized by progressive follicular miniaturization in genetically predisposed individuals. Although the role of androgens, particularly dihydrotestosterone (DHT), is well established[2], increasing evidence suggests that AGA is a multifactorial condition involving inflammatory, vascular, and stromal components[3].

Histological studies have demonstrated the presence of perifollicular microinflammation and progressive fibrosis in affected scalp areas[3]. In addition, alterations of the dermal microenvironment, including extracellular matrix remodeling and changes in the perifollicular adipose compartment, may contribute to follicular dysfunction and miniaturization[2].

Conventional therapies such as 5α-reductase inhibitors and topical minoxidil primarily target hormonal pathways or stimulate hair growth[4,5], but do not directly address microenvironmental alterations. This has led to an increasing interest in regenerative approaches aimed at modulating the follicular niche[6,7].

Autologous adipose-derived micrografts have been proposed as a strategy to improve stromal support and tissue quality[8,9], while polynucleotides (PDRN) have demonstrated anti-inflammatory and pro-angiogenic properties[10,11] mediated through adenosine A2A receptor activation.

The present preliminary case series evaluates the clinical and trichoscopic outcomes of a combined regenerative protocol targeting structural and functional components of the follicular microenvironment in patients with AGA.

Materials and Methods

Study design

This study was designed as a preliminary observational case series evaluating the clinical and trichoscopic outcomes of a regenerative protocol targeting the follicular microenvironment in patients with AGA.

Patient selection

Four patients (two males and two females) with clinically and trichoscopically confirmed AGA were included. Disease severity was classified according to the Norwood–Hamilton scale for male patients and the Ludwig scale for female patients (Figures 1 and 2).

The study population included one male patient with Norwood II AGA, one male patient with Norwood VI AGA, one female patient with Ludwig I–2 AGA, and one female patient with Ludwig I–3 AGA.

Inclusion criteria were clinical and trichoscopic diagnosis of AGA and availability of baseline and 4-month documentation. Exclusion criteria included cicatricial alopecia, active inflammatory scalp disorders, and concomitant AGA treatments. All patients provided a written informed consent.

Treatment protocol

All patients underwent one session of autologous adipose-derived micrografting combined with an intradermal polynucleotide injection, followed by five additional polynucleotide sessions at two-week intervals.

No topical or systemic AGA therapies were administered during follow-up.

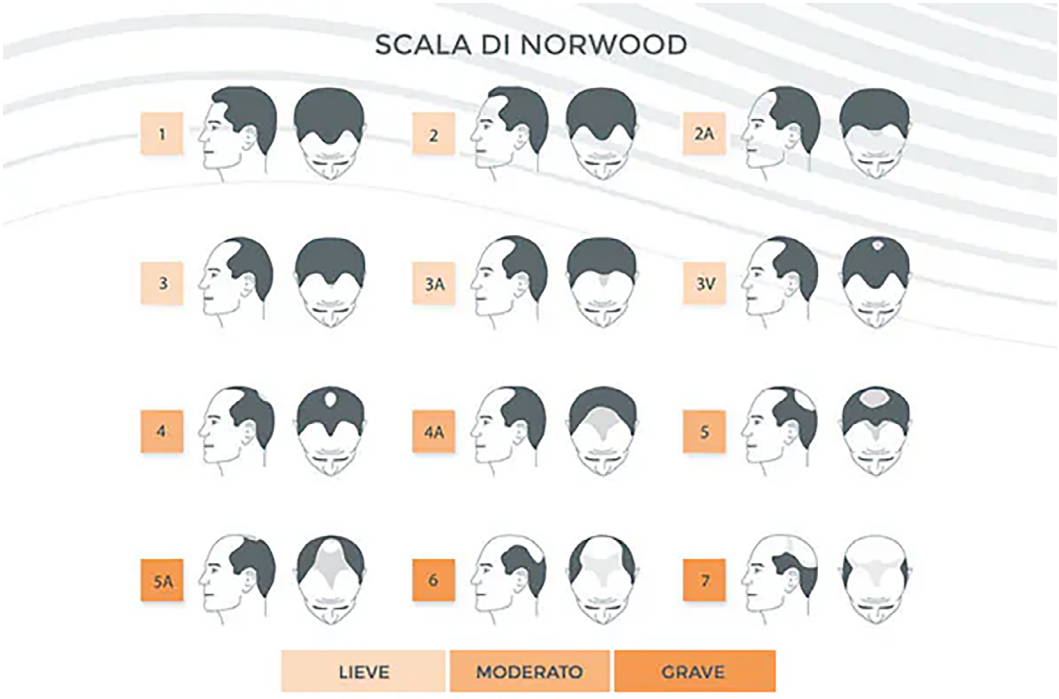

Figure 1. Norwood–Hamilton classification scale for male pattern hair loss.

Figure 2. Ludwig classification scale for female pattern hair loss.

Autologous adipose-derived micrografting

Adipose tissue was harvested under local anesthesia and mechanically processed using a microfragmentation system (SEFFIHAIR®, SEFFILINE S.r.l., Bologna, Italy), without enzymatic digestion.

The processed adipose fraction was injected into the affected scalp areas at deep dermal and subdermal levels.

Polynucleotide treatment

Polynucleotide injections were performed using a commercially available polynucleotide-based medical device (Nucleofill® Medium, Promoitalia S.r.l., Milan, Italy). Polynucleotides exert anti-inflammatory and pro-angiogenic effects through activation of the adenosine A2A receptor and modulation of vascular endothelial growth factor (VEGF) expression.

Outcome assessment

Clinical and trichoscopic evaluations were performed at baseline and at 4 months. Trichoscopic parameters included hair shaft diameter variability, proportion of miniaturized hairs, and apparent hair density[12,13].

Due to the limited sample size, results were analyzed descriptively.

Results

All four patients completed the treatment protocol and follow-up. No adverse events were reported.

Early to intermediate AGA (n = 3)

Three patients demonstrated reduced hair shaft diameter variability and improved apparent density at 4 months. An increased homogeneity of follicular units was observed. Female patients also reported subjective improvement in hair volume and texture.

Advanced AGA (n = 1)

The Norwood VI patient showed mild qualitative improvement characterized by slight increase in hair shaft caliber and stabilization of the clinical picture. No significant increase in density was observed.

Representative baseline and 4-month trichoscopic images are shown in Figures 3-6.

Discussion

AGA has traditionally been interpreted as a hormonally mediated condition[2,14,15]. However, increasing evidence supports a broader pathogenic model involving microinflammation, perifollicular fibrosis[3], and stromal alterations within the scalp microenvironment.

The regenerative protocol adopted in this study targeted both structural and functional components of the follicular niche. Adipose-derived micrografts have been proposed to enhance stromal support and tissue quality[8,9], while polynucleotides exert anti-inflammatory and angiogenic effects[10,11] that may improve local tissue perfusion and cellular metabolism.

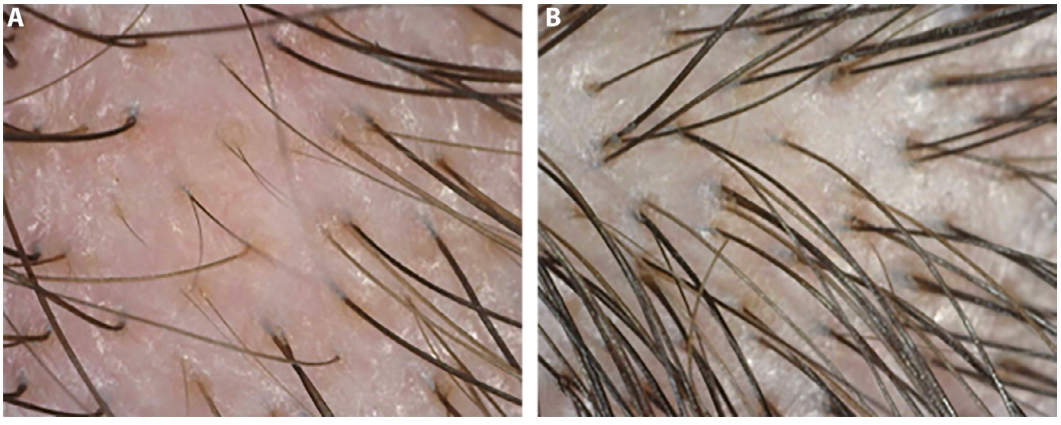

Figure 3. Trichoscopic images of Patient 1 (Norwood II) at baseline (A) and 4 months (B).

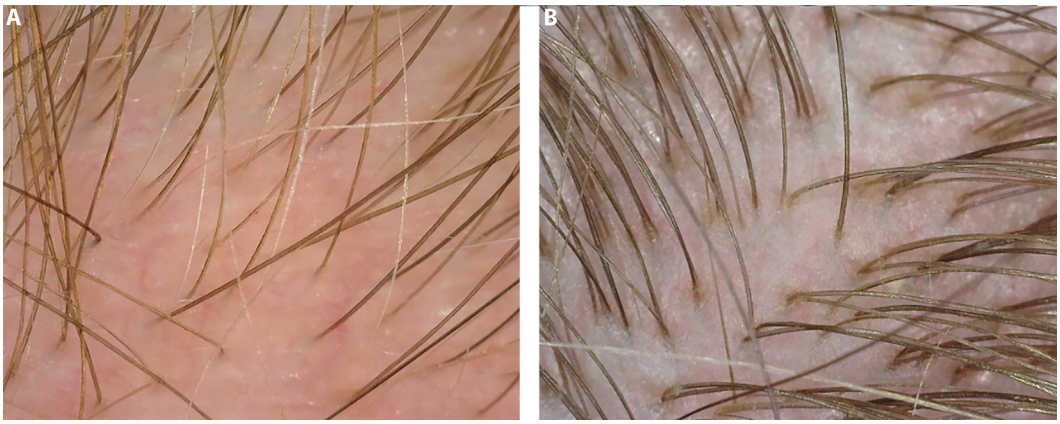

Figure 4. Trichoscopic images of Patient 2 (Ludwig I–2) at baseline (A) and 4 months (B).

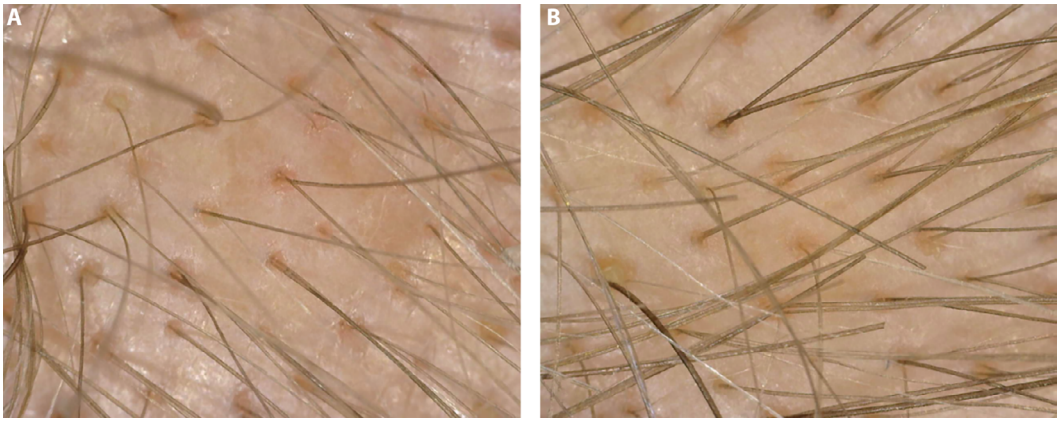

Figure 5. Trichoscopic images of Patient 3 (Norwood VI) at baseline (A) and 4 months (B).

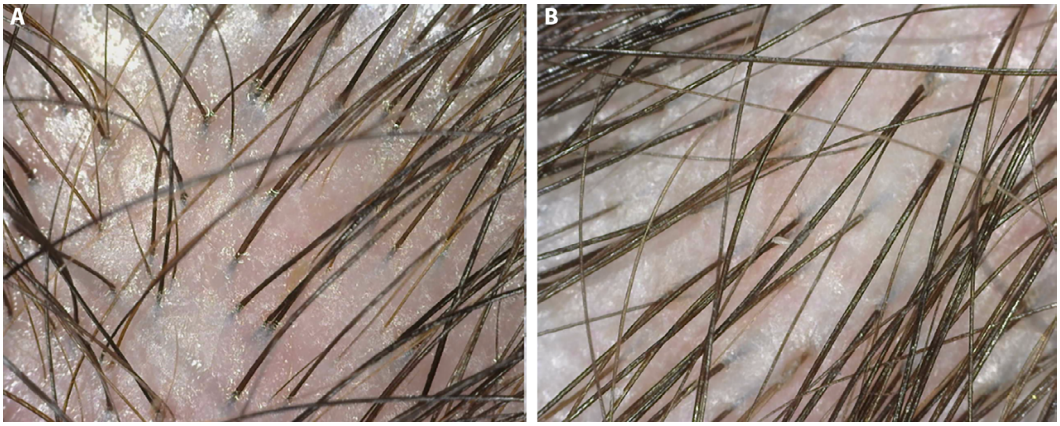

Figure 6. Trichoscopic images of Patient 4 (Ludwig I–3) at baseline (A) and 4 months (B).

The trichoscopic improvements observed in early-stage patients suggest that the modulation of the follicular microenvironment may support partially miniaturized but still viable follicles. Reduced hair shaft diameter variability and improved homogeneity indicate qualitative recovery rather than de novo folliculogenesis.

In contrast, the more limited response in the advanced-stage patient highlights the importance of residual follicular viability. In late-stage AGA, where fibrosis and follicular depletion are more pronounced, microenvironment modulation alone may not be sufficient to induce significant density changes.

The present findings should be interpreted with caution. The limited sample size and observational design preclude definitive conclusions regarding efficacy. Furthermore, the 4-month follow-up may not fully reflect long-term outcomes in a chronic and progressive condition such as AGA.

Nevertheless, the biological plausibility of a microenvironment-targeted strategy supports further controlled investigations with larger patient cohorts and longer follow-up.

Conclusion

This preliminary case series suggests that a regenerative approach targeting the follicular microenvironment through autologous adipose-derived micrografts combined with polynucleotides, may represent a biologically coherent adjunctive strategy in androgenetic alopecia, particularly in early stages where viable follicles are still present.

Further controlled studies are required to better define its clinical role within integrated AGA management.

Ethical Statement: All procedures were performed according to standard clinical practice. A written informed consent was obtained from all patients for treatment and photographic documentation.

Author Contributions: Antonio Luca Amore conceived the study, performed the clinical procedures, collected data, and drafted the manuscript. Basso Di Pasquale contributed to the scientific discussion regarding polynucleotide formulation and critically revised the manuscript. Alessandro Gennai contributed to methodological discussion concerning adipose micrografting techniques and critically revised the manuscript. All authors approved the final version of the manuscript.

Conflict of Interest: Antonio Luca Amore has a professional collaboration agreement with Promoitalia S.r.l. Basso Di Pasquale is Scientific Director of Promoitalia S.r.l. Alessandro Gennai is founder of SEFFILINE S.r.l., manufacturer of the adipose micrografting system used in this study.

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References

1. Sinclair R. Male pattern androgenetic alopecia. BMJ. 1998; 317(7162):865-869.
2. Trüeb RM. Molecular mechanisms of androgenetic alopecia. Exp Gerontol. 2002; 37(8-9):981-990.
3. Whiting DA. Diagnostic and predictive value of horizontal sections of scalp biopsy specimens in male pattern androgenetic alopecia. J Am Acad Dermatol. 1993; 28(5 Pt 1): 755-763.
4. Olsen EA, Messenger AG, Shapiro J, et al. Evaluation and treatment of male and female pattern hair loss. J Am Acad Dermatol. 2005; 52(2):301-311.
5. Gupta AK, Charrette A. The efficacy and safety of 5α-reductase inhibitors in androgenetic alopecia: a network meta-analysis and benefit-risk assessment of finasteride and dutasteride. J Dermatolog Treat. 2014; 25(2):156-161.
6. Gentile P, Garcovich S. Advances in regenerative stem cell therapy in androgenetic alopecia and hair loss: wnt pathway, growth-factor, and mesenchymal stem cell signaling impact analysis on cell growth and hair follicle development. Cells. 2019; 8(5):466.
7. Gentile P, Garcovich S. Systematic review of Platelet-Rich Plasma use in androgenetic alopecia compared with Minoxidil, Finasteride and adult stem cell-based therapy. Int J Mol Sci. 2020; 21(8):2702.
8. Zuk PA, Zhu M, Mizuno H, et al. Multilineage cells from human adipose tissue. Tissue Eng. 2001; 7(2):211-228.
9. Gennai A, Baldessin M, Melfa F, et al. Guided superficial enhanced fluid fat injection (SEFFI) procedures for facial rejuvenation: an italian multicenter retrospective case report. Clin Pract. 2023; 13(4):924-943.
10. Lee S, Zheng Z, Kang J-S, et al. Therapeutic efficacy of autologous platelet-rich plasma ad polydeoxyribonucleotide on female pattern hair loss. Wound Repair Regen. 2015; 23(1):30-36.
11. Colangelo MT, Galli C, Guizzardi S. The effects of polydeoxyribonucleotide on wound healing and tissue regeneration: a systematic review of the literature. Regen. Med. 2020.

12. Rudnicka L, Olszewska M, Rakowska A, Kowalska-Oledzka E, Slowinska M. Trichoscopy: a new method for diagnosing hair loss. J Drugs Dermatol. 2008; 7(7):651-654.
13. Rudnicka L, Rakowska A, Olszewska M. Trichoscopy: how it may help the clinician. Dermatol Clin. 2013; 31(1):29-41.
14. Kaufman KD. Androgen metabolism as it affects hair growth in androgenetic alopecia. Dermatol Clin. 1996; 14(4); 697-711.
15. Randall VA. Androgens and hair growth. Dermatol Ther. 2008; 21(5):314-328.