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Topic: Biologics, immunotherapy, targeted therapy

Paradoxical Alopecia Areata Linked to Adalimumab-atto: case series

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Introduction

Tumor necrosis factor-α (TNF-α) inhibitors are widely used in inflammatory diseases and are generally effective and safe; however, paradoxical immune-mediated adverse events remain incompletely characterized. Adalimumab-atto, a biosimilar of adalimumab, demonstrates comparable efficacy and safety to the originator, yet reports of rare dermatologic paradoxical reactions are scarce. Alopecia areata (AA) is an uncommon and underrecognized paradoxical effect of TNF-α inhibition and has not previously been reported with adalimumab-atto. Borderline paradoxical AA refers to new-onset or worsening AA during TNF-α inhibitor therapy, despite a theoretical immunologic rationale and lack of established therapeutic benefit. A temporal relationship, characteristic trichoscopic findings, and exclusion of alternative causes support a drug-induced mechanism, likely related to disruption of hair follicle immune privilege (1,2). Increased recognition of this phenomenon is essential as biosimilar use expands.

Case Report Objectives and Novelty
- Report the first known case of alopecia areata associated with adalimumab-atto
- Highlight AA as a rare, borderline paradoxical reaction to TNF-α inhibition
- Emphasize diagnostic features supporting a drug-induced mechanism
- Increase clinician awareness of paradoxical reactions with TNF-α biosimilars

Materials and Methods

Patient 1 is a 43-year-old woman with well-controlled hypothyroidism and severe plaque psoriasis (PASI 12) and psoriatic arthritis had a remote history of a single self-resolving episode of patchy alopecia areata (AA) eight years earlier . Family history was notable for vitiligo and psoriasis. She achieved sustained psoriasis control with ustekinumab and narrowband UVB phototherapy. After three years, ustekinumab was discontinued for financial reasons and replaced with adalimumab-atto. Six weeks later, she developed new-onset non-scarring patchy alopecia of the left parietal and vertex scalp, accompanied by worsening psoriasis. Trichoscopy showed yellow and black dots, exclamation-mark hairs, and short vellus hairs without scarring or scale **(Figure 1. A-D).** Adalimumab-atto was discontinued, and topical clobetasol propionate 0.05% ointment was initiated.

Patient 2 is a 10-year-old boy with immune thrombocytopenia was followed for erythrodermic juvenile pityriasis rubra pilaris (PRP). There was no personal or family history of AA, psoriasis, or other autoimmune disease. His disease was refractory to oral corticosteroids, cyclosporine, and acitretin but achieved control for 43 weeks with ustekinumab, which was discontinued due to financial constraints. After relapse, adalimumab-atto was initiated in combination with cyclosporine. Eight weeks later, he developed new-onset patchy, non-scarring alopecia of the vertex scalp without nail or other hair involvement. Trichoscopy revealed yellow dots and short vellus hairs **(Figure 1. E-F).** Adalimumab-atto was continued with close monitoring, cyclosporine was tapered and discontinued, and topical therapy for alopecia with

alternating mometasone furoate lotion and tacrolimus 0.1% ointment was started.

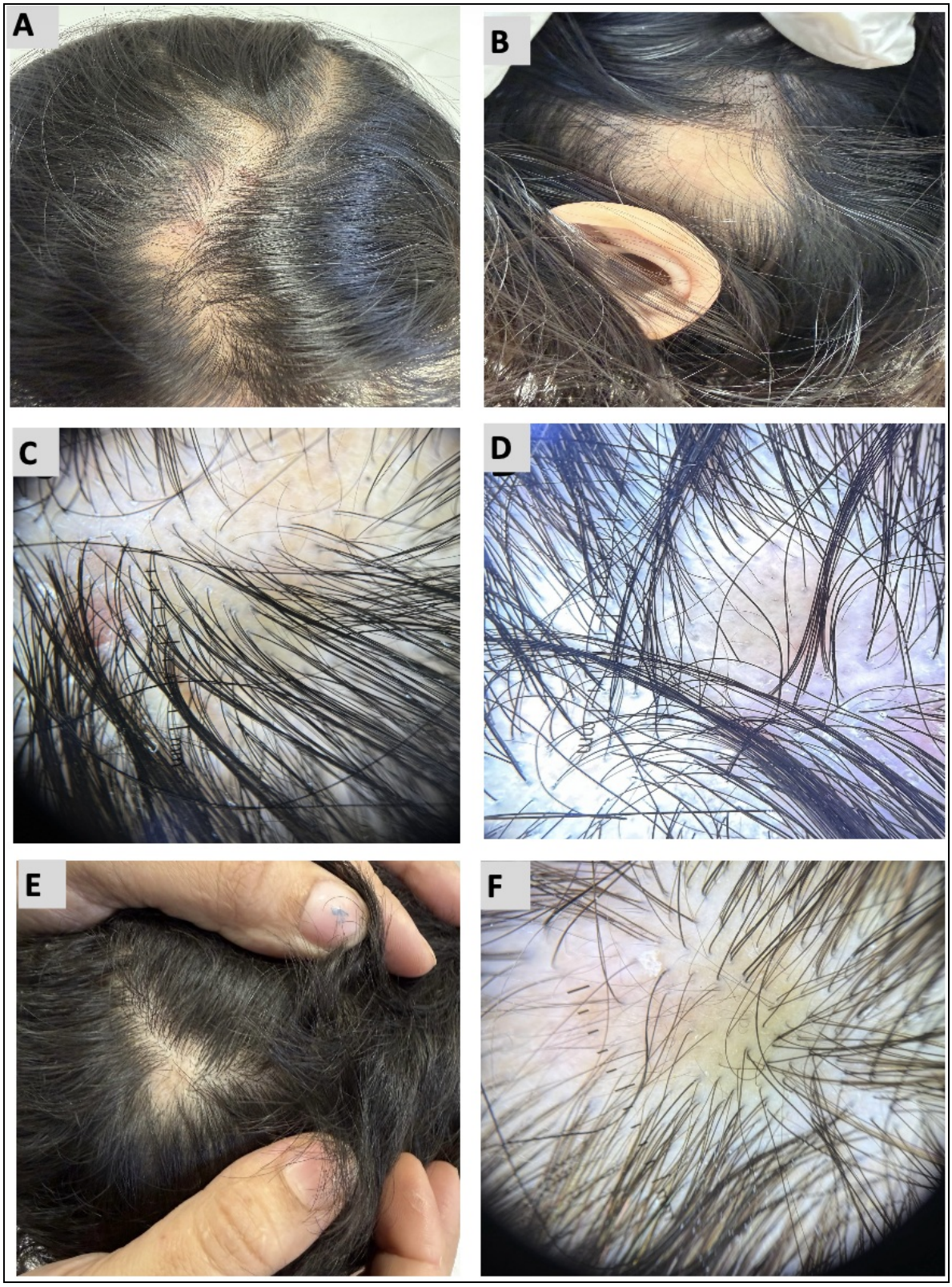


Figure 1. Clinical and trichoscopic features of paradoxical alopecia areata associated with adalimumab-atto. (A–D) Patient 1: Clinical photographs show well-demarcated, non- scarring alopecic patches involving the left parietal and occipital scalp, with smooth, normal-appearing skin, preserved follicular openings, and absence of scale, erythema, or psoriasiform inflammation. Trichoscopic examination reveals multiple yellow dots corresponding to dilated follicular ostia filled with keratin and sebum, along with black dots, exclamation-mark hairs, and short regrowing vellus hairs, consistent with active alopecia areata. (E–F) Patient 2: Clinical image demonstrates a localized, well- circumscribed, non-scarring alopecic patch over the vertex scalp with normal underlying skin and no inflammatory or scaly changes. Trichoscopy shows yellow dots and numerous short vellus hairs, compatible with alopecia areata in an early regrowth phase, without features of psoriasiform or cicatricial alopecia. Examination of the palms reveals diffuse, symmetric, yellow-orange waxy

hyperkeratosis with accentuated skin markings, consistent with palmoplantar involvement of pityriasis rubra pilaris, and the trunk and neck demonstrate controlled pityriasis rubra pilaris at the time of alopecia onset.

Results

N/A

Conclusions

- Borderline paradoxical alopecia areata is a rare but clinically significant immune-mediated adverse effect of TNF-α inhibitors, including the biosimilar adalimumab-atto
- Early recognition of new-onset hair loss enables prompt evaluation and individualized risk–benefit assessment
- Awareness of this paradoxical reaction supports informed therapeutic decision-making and optimized patient outcomes
- Increased clinician recognition is essential as biologic and biosimilar use continues to expand