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Single Case

Alopecia Diffusa while Using Interleukin-17 Inhibitors against Psoriasis Vulgaris

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Keywords
Alopecia diffusa · Interleukin-17 · Psoriasis vulgaris · Th17 cells · Th1 cells

Abstract
We report two cases of alopecia diffusa during the treatment of psoriasis vulgaris with interleukin (IL)-17 inhibitors. Psoriasis is one of the most common immune-mediated chronic skin diseases, strongly associated with IL-17A. Clinically, the monoclonal antibodies to IL-17A or its receptor, IL-17R, show a dramatic effect against psoriasis. Alopecia is also an IL-17-mediated autoimmune disease, and IL-17 inhibitors have been expected to be the gold standard for the treatment of alopecia; therefore, the complication of alopecia while using IL-17 may be regarded as an unexpected "paradoxical reaction." T helper (Th)17 cells are not cytotoxic enough by themselves to undermine the hair follicle under normal circumstances, they need the coexistence of CD8+ cytotoxic Th1 cells. Th17 cells may be the initiator of the damage of the hair follicle, but CD8 T cells or more powerful Th1 cells are required as followers. The Th17/Th1 axis might convert into a Th1-dominant immune status using IL-17 inhibitors, and the destruction of the hair follicle might result in alopecia. An accumulation of cases is to be expected.

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Introduction

Psoriasis is one of the most common immune-mediated chronic skin diseases characterized by aberrant hyperproliferative keratinocytes and a dysregulation of immune cell infiltrates into the skin. Interleukin (IL)-17A is the key cytokine in psoriasis synergistically enhancing with IL-22, and it contributes to hyperkeratosis. Clinically, the monoclonal antibodies to IL-17A or its receptor, IL-17R, show a dramatic effect against psoriasis. We here report two cases of alopecia diffusa while using IL-17 inhibitors against psoriasis vulgaris.

Case Presentation

A 62-year-old female visited our department for the treatment of moderate psoriasis vulgaris of 2 years. Six months after starting secukinumab, an IL-17 A inhibitor, alopecia diffusa began to cover her whole scalp (Fig. 1a), although her skin symptoms due to psoriasis had completely disappeared by then. Her medication was switched to brodalumab, an IL-17R antagonist, but her loss of hair continued. Then, 10 mg oral prednisolone was supplemented, and this stopped her loss of hair and she recovered from her alopecia (Fig. 1b). Psoriasis is also well-controlled until today. Her antinuclear antibody test was negative.

Our other patient was a 40-year-old female with the history of breast cancer. Moderate type psoriasis vulgaris had occurred 12 years ago, and we treated her with brodalumab. Her skin eruption disappeared quickly, but alopecia diffusa started after 2 months (Fig. 1c). We changed her medication to ustekinumab, an IL-12/23 p40 inhibitor, and her hair recovered without the administration of oral immune suppressants (Fig. 1d). No relapse of alopecia has been observed. Her antinuclear antibody test was negative.

Discussion

From a pathogenetic viewpoint, IL-17 and its main source of T helper (Th)17 cells are one of the critical inducers of alopecia [1]. Abundant amounts of Th17 cells cause damage of the hair follicle, and high plasma IL-17 levels are detected in patients with alopecia. An IL-17 inhibitor has been expected to be the gold standard for the treatment of alopecia; therefore, the complication of alopecia while using IL-17 may be regarded as an unexpected "paradoxical reaction."

Th17 cells are not cytotoxic enough by themselves to undermine the hair follicle under normal circumstances, they need the coexistence of CD8+ cytotoxic Th1 cells. A similar pattern is recognized in the joint of psoriatic arthritis (PsA) patients. Although psoriasis and PsA are Th17-mediated disorders, PsA joint fluid is enriched for IL-17+CD8 T cells, and the level of this T-cell subset correlates significantly with disease activity [2]. In addition, PsA synovium is enriched for proinflammatory cytokines such as TNF-α, IL-1β, and IL-6 [3]. Therefore, Th17 may be the initiator of the damage of the hair follicle, but CD8 T cells or more powerful Th-type cells, such as Th1, are required as followers. IFN-γ+CD8 T cells are abundant in alopecia skin lesions [4]. The Th17/Th1 axis might convert into a Th1-dominant immune status using IL-17 inhibitors, and the destruction of the hair follicle might result in alopecia. An accumulation of cases is to be expected.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors declare that no competing interests exist.

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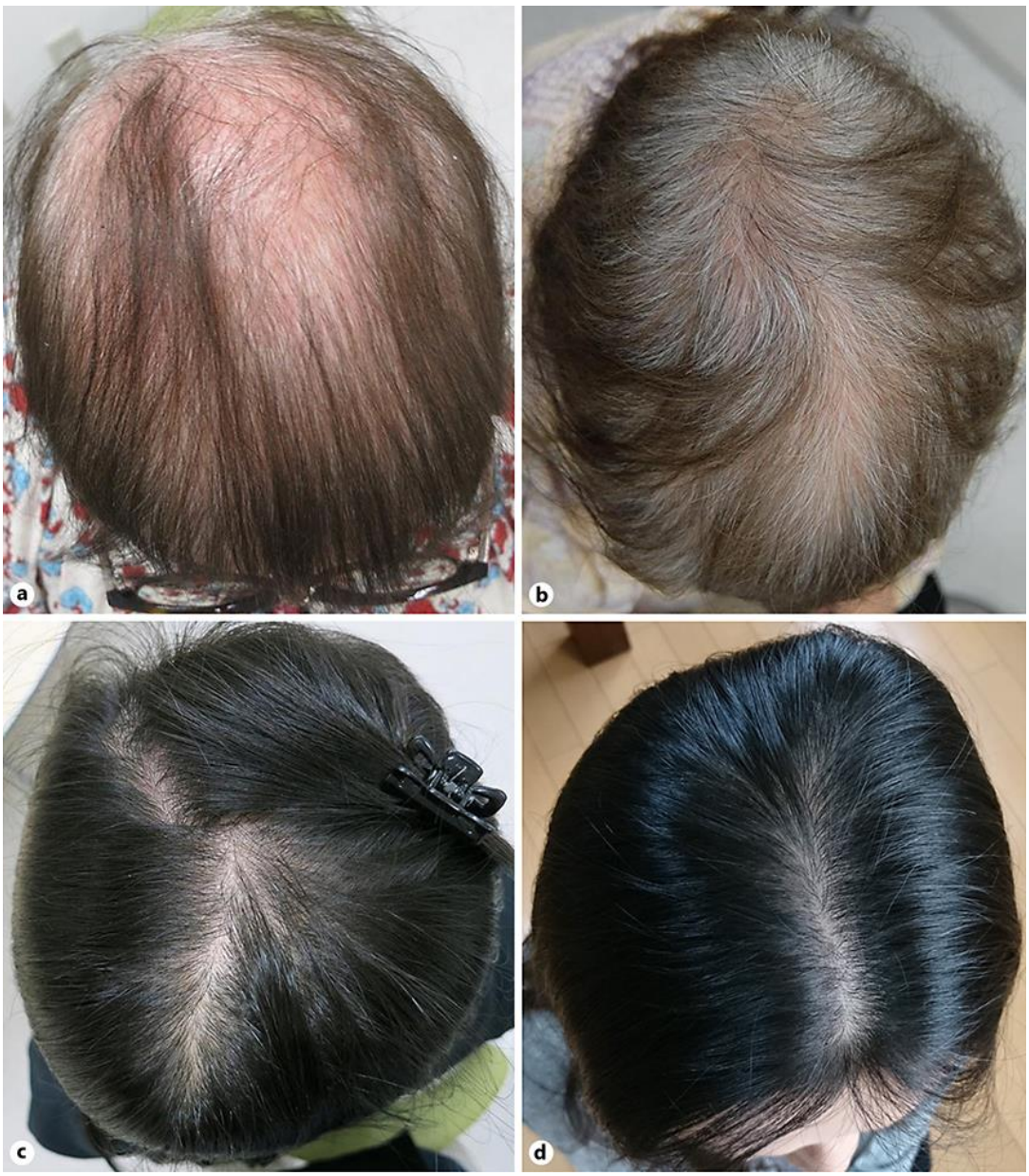

Fig. 1. Clinical findings. **a**, **b** Patient 1. Diffuse hair loss started covering her whole scalp 6 months after starting secukinumab for the treatment of moderate type psoriasis vulgaris (**a**). Hair loss was stopped and the patient recovered from alopecia by the supplementation of 10 mg oral prednisolone (**b**). **c**, **d** Patient 2. Alopecia diffusa started after 2 months of brodalumab treatment for moderate type psoriasis vulgaris (**c**). The patient's medication was changed to ustekinumab, and her hair recovered without the administration of oral immune suppressants (**d**).