

Clinical Letter

Simultaneous effectiveness of dupilumab in atopic dermatitis and alopecia areata in two patients

DOI: 10.1111/ddg.13990

Dear Editors,

Alopecia areata (AA) is a fairly common, non-cicatricial type of hair loss with an estimated lifetime incidence of 2.1 % and an epidemiological association with atopy [1–3]. The clinical presentation can vary from small, well-circumscribed round or oval alopecic patches to a complete absence of scalp hair in alopecia totalis (AT) or of the entire scalp and body hair in alopecia universalis (AU). Despite the relatively high prevalence of AA, the therapeutic armamentarium of topical/intralesional corticosteroids, topical dithranol or diphenylcyclopropenone, systemic corticosteroids and photochemotherapy is often insufficient, especially in extensive or long-standing AA [4, 5].

We report two cases highlighting the dual effectiveness of dupilumab in AA and atopic dermatitis (AD).

Case 1 is a 38-year-old male who presented to our dermatology department for management of his moderate to severe atopic dermatitis, which he had had since the age of three years. He also had associated allergic rhinoconjunctivitis (ARC) and asthma, currently treated with reproterol/cro-

moglycate and salbutamol. In addition, he had a history of alopecia universalis for five years. Previous treatments of AD included UVB 311 nm phototherapy followed by cyclosporine (max. 4.72 mg/kg body weight [bw]). However, due to generalized myalgia the cyclosporine dose was reduced to 2.0 mg/kg body weight, which led to frequent AD exacerbations.

Physical examination at presentation demonstrated multiple eczematous patches affecting the back, upper and lower extremities, as well as hyperkeratotic hand eczema. The corresponding atopic dermatitis score (SCORAD) was 27. He also had complete hair loss of the body and scalp, with only a few eyebrow hairs left (Figure 1a). Cyclosporine was stopped and the patient was then started on dupilumab at 600 mg subcutaneously on day 0, followed by 300 mg subcutaneously every two weeks. The patient noticed the first hair re-growth four weeks after initiation of dupilumab treatment. At week 22 of dupilumab treatment, a few eczematous patches on the back and upper extremities as well as the hyperkeratotic hand eczema persisted, while the corresponding SCORAD score had improved to 16. The scalp, eyelashes and eyebrows also showed significant hair re-growth (Figure 1b).

Case 2 is a 32-year-old male with severe atopic dermatitis since the age of two, with concomitant ARC and asthma (which was treated with salbutamol on demand). He also had ophiasis-type AA for two years. Previous treatments of AD included repeated sessions of UVA1 phototherapy followed by cyclosporine (max. 2.3 mg/kg bw) and azathioprine (max. 2.5 mg/kg bw); the latter two were discontinued due to abdominal pain and recurrent infections, respectively.

Physical examination four weeks after cessation of the UVA1 phototherapy demonstrated multiple eczematous

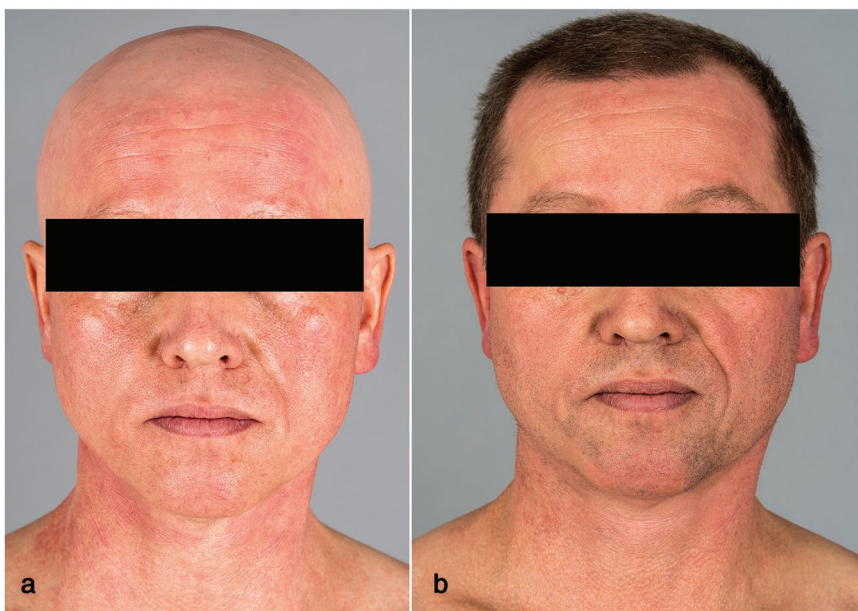


Figure 1 Patient 1 with concomitant atopic dermatitis (AD) and alopecia universalis (AU) involving the scalp, eyebrows, eyelashes and beard before treatment (a) and at week 22 after initiating dupilumab therapy (b).



Figure 2 Patient 2 with concomitant atopic dermatitis (AD) affecting the scalp, as well as alopecia areata (AA) affecting the occiput. Before treatment (a) and at week 21 after initiating dupilumab therapy (b).

patches affecting the back, scalp, upper and lower extremities, as well as multiple excoriated nodules on the upper and lower extremities, as well as occipital AA of the ophiasis type (Figure 2a). The corresponding SCORAD score was 41. The patient was started on dupilumab with the approved standard as mentioned above. At week 12 of dupilumab treatment, he had non-pigmented hair in the previously alopecic areas, and the corresponding SCORAD score was 27. At week 21 his hair was almost fully regrown and pigmented (Figure 2b), and the corresponding SCORAD score had improved further to 17, with significant flattening of the nodules on the extremities.

Although the exact pathogenesis of AA is still incompletely understood, potential causes include a loss of immune privilege in the hair follicle, autoimmune-mediated hair follicle destruction, and upregulation of inflammatory pathway [6]. While AA has previously been assigned to the Th1 category [4], recent data show heterogeneity of immune pathway dysregulation in the development of AA, with additional involvement of the Th2 cytokines IL-4 and IL-13, Th17/IL-23 and phosphodiesterase-4 (PDE4) pathways [2, 5, 7]. Furthermore, the pathogenic relevance of Th2 axis involvement is supported by the epidemiological association of AA with atopy, a classic Th2 condition [4].

Dupilumab shows efficacy with both AD and asthma, and has recently been approved for treatment of moderate to severe AD [7]. It is a fully humanized monoclonal antibody that antagonizes the IL-4-receptor α (IL-4Ra) subunit, impeding both IL-4 and IL-13 signaling. Our case shows that dupilumab can also be effective with alopecia areata, and supports the pathogenic relevance of IL-4 and IL-13 in AA.

However, a temporal relationship between the administration of dupilumab and subsequent development of AA was also reported recently [8]. Further studies are therefore needed to elucidate the exact pathogenesis of AA and to develop targeted therapies for AA.

In summary, patients suffering from AA in association with AD might benefit from treatment with dupilumab in a surprisingly short time, even after many years of total hair loss, and this may improve their quality of life considerably. We therefore confirm case reports of other authors on this topic [9, 10]. However, the long-term efficacy of dupilumab is still unknown.

Conflict of interest

None.

**Laine Ludriksone, Peter Elsner,
Sibylle Schliemann**

Department of Dermatology, University Hospital Jena,
Jena, Germany

Correspondence to

Laine Ludriksone
Department of Dermatology
University Hospital Jena

Erfurter Strasse 35
07743 Jena, Germany

E-mail: laine.ludriksone@med.uni-jena.de

References

- 1 Mirzoyev SA, Schrum AG, Davis MDP et al. Lifetime incidence risk of alopecia areata estimated at 2.1 % by Rochester Epidemiology Project, 1990–2009. *J Invest Dermatol* 2014; 134: 1141–2.
- 2 Song T, Pavel AB, Wen HC et al. An integrated model of alopecia areata biomarkers highlights both TH1 and TH2 upregulation. *J Allergy Clin Immunol* 2018; 142(5):1631–4.
- 3 Werfel T, Heratizadeh A, Aberer W et al. S2k guideline on diagnosis and treatment of atopic dermatitis—short version. *J Dtsch Dermatol Ges* 2016; 14: 92–106.
- 4 Wang ECE, Christiano AM. The changing landscape of alopecia areata: the translational landscape. *Adv Ther* 2017; 34: 1586–93.
- 5 Renert-Yuval Y, Guttman-Yassky E. The changing landscape of alopecia areata: the therapeutic paradigm. *Adv Ther* 2017; 34: 1594–609.
- 6 Strazzulla LC, Wang EHC, Avila L et al. Alopecia areata: Disease characteristics, clinical evaluation, and new perspectives on pathogenesis. *J Am Acad Dermatol* 2018; 78: 1–12.
- 7 Malik K, Guttman-Yassky E. Cytokine targeted therapeutics for alopecia areata: lessons from atopic dermatitis and other inflammatory skin diseases. *J Invest Dermatol Symp Proc* 2018; 19: S62–4.
- 8 Mitchell K, Levitt J. Alopecia areata after dupilumab for atopic dermatitis. *JAAD Case Rep* 2018; 4: 143–4.
- 9 Darrigade AS, Legrand A, Andreu N et al. Dual efficacy of dupilumab in a patient with concomitant atopic dermatitis and alopecia areata. *Br J Dermatol* 2018; 179: 534–6.
- 10 Penzi LR, Yasuda M, Manatis-Lornell A et al. Hair regrowth in a patient with long-standing alopecia totalis and atopic dermatitis treated with dupilumab. *JAMA Dermatology* 2018; 154: 1358–60.