

## Massive Acute Alopecia of the Scalp in a Patient Treated with Dupilumab

Rosella GALLO, Iliara TRAVE and Aurora PARODI

Section of Dermatology - Department of Health Sciences, University of Genoa, Ospedale Policlinico San Martino – IRCCS, Genoa, Italy.  
E-mail: rs.gallo@unige.it

Accepted May 28, 2020; Epub ahead of print Jun 8, 2020

Dupilumab is the first targeted biological therapy approved for the treatment of adult patients with moderate-to-severe atopic dermatitis (AD). It is a human monoclonal antibody that targets the alpha subunit of the interleukin (IL)-4 receptor shared by both IL-4 and IL-13, which are secreted by CD4<sup>+</sup> lymphocytes. Its main adverse effects include injection site reactions, nasopharyngitis and conjunctivitis (1). Although it has been reported to improve alopecia areata (AA) (2) there have been increasing reports of AA and AA-like reactions in patients with AD treated with dupilumab (2–12). We report here a patient who developed massive hair shedding, mimicking AA, after 8 weeks of starting dupilumab.

### CASE REPORT

A 24-year-old man, with neither family nor personal history of AA or psoriasis, presented with severe adult-onset AD of 5-year duration that was recalcitrant to topical corticosteroids and systemic, 3 mg/kg/day, ciclosporin. Further to a diagnosis of ulcerative colitis, he had also been taking 10 mg/day prednisolone and 800 mg ×3/day salazopyrin for one year. His Eczema Area and Severity Index (EASI) score was 24. Hence, after a loading dose of 600 mg, dupilumab, 300 mg subcutaneously, was started, while ciclosporine and prednisolone were tapered and stopped. The patient experienced rapid improvement in his AD. However, after 6 weeks he developed dermatitis suggestive of inverse psoriasis in the armpits, navel and intergluteal cleft, associated with erythema and scaling

of the scalp. Itraconazole, 200 mg/day, and an antifungal/corticosteroid medication induced remission of the psoriasis-like lesions on the body within 10 days. However, the scalp dermatitis persisted and 8 weeks after starting dupilumab the patient developed abrupt shedding of hair on the entire scalp, with tufts of hair held together by conglomerated scales or casts, on a background of diffuse erythema and scaling (SALT (Severity of Alopecia Tool) scored 71.6) (Fig. 1). Topical clobetasol was started and dupilumab was continued until 4 weeks later, when both his atopic dermatitis and alopecia worsened (Fig. 1d). The patient declined a biopsy of the scalp. Dupilumab was then discontinued and ciclosporin, 3 mg/kg/day, was re-started. Within 4 weeks, the patient experienced partial hair regrowth and his AD improved. After 3 months, hair regrowth was complete.

### DISCUSSION

To the best of our knowledge, 13 patients who developed abrupt shedding of hair following treatment with dupilumab have been reported in literature (2–12) to date. They include 2 different patterns of alopecia: classic AA (2–8) and AA-like hair loss associated with erythema and scaling (10–14). Table S1<sup>1</sup> shows the main characteristics of these patients.

<sup>1</sup><https://doi.org/10.2340/00015555-3549>



**Fig. 1. Patient's scalp.** (a) Baseline; (b) 8 weeks after starting dupilumab; (c) tufts of hair held together by conglomerated scales or casts; (d) 12 weeks after starting dupilumab, diffuse hair loss on a background of erythema and scaling.

Classic AA was reported in 8 patients (5 men and 3 women, 20–51-year age range). The diagnosis was based on both clinical and dermatoscopic features in one patient (5) and on clinical features only in 7 (2–4, 6–8). None of the patients was biopsied. A history of previous AA was present in 2 patients (3, 4), absent in 4 (2, 7, 8), and not reported in 2 (5, 6). All of the patients had severe atopic dermatitis that markedly improved with dupilumab. The time lapse between starting dupilumab and the onset of AA ranged between 2 days and 28 months. Dupilumab was discontinued in 2 patients (3, 7) and continued in 5 (3–6, 8). In one case, the authors do not report whether the drug was continued (4). All patients experienced hair regrowth within 3 weeks to 6 months.

AA-like reactions, characterized by abrupt shedding of hair, associated with erythema and scaling, as in the current case, were reported in 5 patients (5 men, 27–33 years) who were affected by severe AD that greatly improved on dupilumab. A personal or family history of AA was absent in 4 (8–10, 12) and unknown in one patient (11). In 4 out of 5 patients, histology was performed, showing psoriasiform epidermal features and alopecia areata-like dermal changes (Table S1<sup>1</sup>). Alopecia developed within 5–7 weeks of starting dupilumab in 3 patients (9, 10, 12), and within 18–40 weeks in 2 patients (8–11). Dupilumab was withdrawn in 2 patients and continued in 3 patients. Hair regrowth of different degrees was reported in 4 patients (8, 9, 11, 12).

Although it cannot be proven on histological grounds, the clinical characteristics and timing of the alopecia in the current patient are highly suggestive of a psoriatic-like reaction induced by dupilumab. His alopecia developed shortly after starting the drug, was not responsive to potent topical steroids, and resolved after discontinuation of dupilumab and the reintroduction of cyclosporine. It is noteworthy that a transient body dermatitis resembling inverse psoriasis had preceded his alopecia.

IL-4 is a known negative regulator of Th1- and Th17-mediated inflammation. It has been suggested that its blockade by dupilumab may create a Th2/Th1 imbalance and enhance or promote Th1/Th17. This imbalance may increase expression of interferon-gamma (13) causing skin manifestations, such as psoriasis (14), psoriatic alopecia (15) and paradoxical psoriasiform reactions (16). Moreover, expression of IL4 and IL13 is correlated with the development of sebaceous glands, and it has been suggested that alterations in the expression of these factors may cause sebaceous gland atrophy (17). Our case seems to confirm this hypothesis. Some AA-like reactions occurring during treatment with dupilumab (17) may, in

fact, be forms of psoriatic alopecia, i.e. an uncommon entity that has also been reported as a possible side-effect of anti-tumour necrosis factor- $\alpha$  therapy (18).

## REFERENCES

- Fabbrocini G, Napolitano M, Megna M, Balato N, Patrino C. Treatment of atopic dermatitis with biologic drugs. *Dermatol Ther* 2018; 8: 527–538.
- Yazdanyar S, Jemec GBE. Alopecia areata after treatment with dupilumab. *Dermatitis* 2019; 30: 175–176.
- Chung J, Slaughter CL, Simpson EL. Alopecia areata in 2 patients treated with dupilumab: New onset and worsening. *JAAD Case Rep* 2019; 5: 643–645.
- Carnicle JM, Hendricks AJ, Shi VY. Reactivation of alopecia areata after dupilumab therapy for atopic dermatitis. *Dermatitis* 2019 Aug 21 (Epub ahead of print).
- Kanda N, Koto M, Hoashi T, Saeki H. Case of alopecia areata during dupilumab treatment for atopic dermatitis. *J Dermatol* 2019; 46: 332–333.
- Patrino C, Napolitano M, Ferrillo M, Fabbrocini G. Dupilumab and alopecia: a Janus effect. *Dermatol Ther* 2019; 32: 13023.
- Barbarin C, Hosteing S, Nosbaum A, Allouchery M, Celerier P. Early onset of alopecia areata after dupilumab introduction in a patient with atopic dermatitis. *Eur J Dermatol* 2019; 29: 542–543.
- Zhu GA, Kang KJW, Chen JK, Novoa RA, Brown RA, Chiou AS, et al. Inflammatory alopecia in patients on dupilumab: a retrospective cohort study at an academic institution. *J Eur Acad Dermatol Venereol* 2020; 34: e159–e161.
- Mitchell K, Levitt J. Alopecia areata after dupilumab for atopic dermatitis. *JAAD Case Rep* 2018; 4: 143–144.
- Barroso-García B, Rial MJ, Molina A, Sastre J. Alopecia areata in severe atopic dermatitis treated with dupilumab. *J Investig Allergol Clin Immunol* 2018; 28: 420–421.
- Flanagan K, Sperling L, Lin J. Drug-induced alopecia after dupilumab therapy. *JAAD Case Rep* 2018; 5: 54–56.
- Salgüero-Fernández I, Gonzalez de Domingo MA, Suarez D, Roustán-Gullón G. Dermatitis and alopecia in a patient treated with dupilumab: a new adverse effect? *Clin Exp Dermatol* 2019; 44: 41–43.
- Brøgger P, Blom LH, Simonsen S, Thyssen JP, Skov L. Antagonism of the interleukin 4 receptor  $\alpha$  promotes TH1-signalling among T cells from patients with atopic dermatitis after stimulation. *Scand J Immunol* 2020; 91: e12835.
- Varma A, Levitt J. Dupilumab-induced phenotype switching from atopic dermatitis to psoriasis. *JAAD Case Rep* 2020 19; 6: 217–218.
- Ruano J, Suárez-Fariñas M, Shemer A, Oliva M, Guttman-Yassky E, Krueger JG. Molecular and cellular profiling of scalp psoriasis reveals differences and similarities compared to skin psoriasis. *PLoS One* 2016; 11: e0148450.
- Stoffel E, Maier H, Riedl E, Brügggen MC, Reininger B, Schaschinger M, et al. Analysis of anti-tumour necrosis factor-induced skin lesions reveals strong T helper 1 activation with some distinct immunological characteristics. *Br J Dermatol* 2018; 178: 1151–1162.
- Maloney NJ, Worswick S, Cheng K. Development of alopecia in patients treated with dupilumab. *Dermatol Ther* 2019; 32: 12869.
- Doyle LA, Sperling LC, Baksh S, Lackey J, Thomas B, Vleugels RA, et al. Psoriatic alopecia/alopecia areata-like reactions secondary to anti-tumor necrosis factor- $\alpha$  therapy: a novel cause of noncicatricial alopecia. *Am J Dermatopathol* 2011; 33: 161–166.