

LETTER TO THE EDITOR

Development of alopecia in patients treated with dupilumab

Dear Editor,

Dupilumab is an FDA-approved interleukin (IL)-4 receptor subunit α (IL-4R α) inhibitor with approval for atopic dermatitis and asthma. Dupilumab is considered a relatively safe drug with few serious adverse effects but is linked to conjunctivitis in patients with atopic dermatitis. Recently, four case reports have described alopecia in patients shortly after beginning dupilumab therapy for atopic dermatitis. We sought to briefly review these cases.

Each of the four reported patients had severe atopic dermatitis at baseline which markedly improved on dupilumab. Three of these patients developed alopecia between Weeks 5 and 7 of dupilumab administration (Table 1) (Barroso-Garcia et al., 2018; Flanagan et al., 2018; Mitchell & Levitt, 2018; Salguero-Fernández et al., 2019). A different set of three patients also had erythema or scaling overlying their alopecia, which developed simultaneously with the alopecia (verified by personal communication). These patients each received scalp biopsies, and all had typical histological findings of alopecia areata. However, additional findings atypical of classic alopecia areata including sebaceous gland atrophy, apoptotic keratinocytes, and a plasma cell infiltrate (with negative treponemal and nontreponemal testing) in the dermis with marked spongiosis, and epidermal parakeratosis and spongiosis were also present (Table 1) (Peckham, Sloan, & Elston, 2011). One of the four patients

discontinued dupilumab after developing alopecia, with subsequent recovery of hair regrowth. Two patients who continued dupilumab received topical or intralesional steroids for their alopecia and also experienced hair regrowth, and the outcome of the last patient was unknown (Barroso-Garcia et al., 2018; Flanagan et al., 2018; Salguero-Fernández et al., 2019). A family history of alopecia was negative in one case (Barroso-Garcia et al., 2018), and not described in any other case report.

The development of alopecia with simultaneous overlying scalp dermatitis and biopsy findings atypical of alopecia areata suggests a phenotype distinct from classic alopecia areata. If these cases truly represent alopecia areata-like reactions secondary to dupilumab, it would seem somewhat paradoxical since dupilumab has successfully treated patients with alopecia areata, and a placebo controlled randomized trial is in progress to evaluate its efficacy for this indication (ClinicalTrials.gov, 2018; Penzi, Yasuda, Manatis-Lornell, Hagigeorges, & Senna, 2018). However, a similar phenomenon has been described in patients receiving tumor necrosis factor (TNF)- α inhibitors who develop psoriatic plaques on the scalp with concomitant noncicatricial alopecia. Biopsies in these cases demonstrate unique histological features compared to both alopecia areata and primary psoriatic alopecia (Doyle et al., 2011). Some of these patients experienced hair regrowth while continuing their

TABLE 1 Characteristics of patients with alopecia after receiving dupilumab for atopic dermatitis

Age/sex	Clinical characteristics/ estimated SALT score	Time from dupilumab to onset of alopecia	Biopsy	Withdrawal of dupilumab	Alopecia treatment	Clinical course	Reference
29/M	+ patchy scalp alopecia No scalp erythema/scaling SALT = 20	5 weeks	No	No	Intralesional triamcinolone	Slow improvement in hair growth	Mitchell and Levitt (2018)
27/M	+ patchy scalp alopecia +scalp scaling/erythema SALT = 20	18 weeks	Yes ^a	Yes	Intralesional and topical triamcinolone, topical tacrolimus	Hair growth recovery within 8 weeks	Flanagan, Sperling, and Lin (2018)
33/M	+ patchy alopecia of scalp and beard area + scalp dermatitis SALT = 42	7 weeks	Yes ^b	No	Topical mometasone	Resolution of scalp dermatitis first, subsequent hair regrowth at 3 months	Salguero-Fernández, Gonzalez de Domingo, Suarez, and Roustan- Gullón (2019)
31/M	+ patchy scalp alopecia + scalp dermatitis SALT = 4	6 weeks	Yes ^c	No	Intralesional triamcinolone	Unknown	Barroso-Garcia, Rial, Molina, and Sastre (2018)

Note. SALT: severity of alopecia tool.

^aSevere sebaceous gland atrophy in addition to typical histological findings of alopecia areata including hair miniaturization and peribulbar chronic inflammation.

^bEpidermal spongiosis with parakeratosis and apoptotic keratinocytes, lymphocytic infiltrate and plasma cells in papillary dermis, in addition to typical histological findings of alopecia areata.

^cSuggestive of alopecia areata, also with epidermal areas of inflammation with exocytosis, spongiosis, and parakeratosis.

TNF inhibitor after receiving intralesional and topical steroids (Doyle et al., 2011). In this case, the alopecia is attributed to dysregulated overproduction of interferon- γ secondary to TNF blockade (Doyle et al., 2011). Similarly, dupilumab could also alter immune signaling, triggering alopecia areata, and dermatitis. IL-4 is a known negative regulator of Th1 and Th17 mediated inflammation; its blockade by dupilumab may upregulate Th1 and Th17 pathways, which play a role in alopecia areata pathogenesis (Lazarski, Ford, Katzman, Rosenberg, & Fowell, 2013; Renert-Yuval & Guttman-Yassky, 2017).

The potential for alopecia and accompanying scalp dermatitis in response to dupilumab should be considered by dermatologists prescribing dupilumab. However, further monitoring will be necessary to assess the likelihood that an alopecia areata-like reaction is a true rare adverse effect of dupilumab. If so, whether this effect is unique to patients with atopic dermatitis or more likely in those with worse baseline atopic dermatitis are questions for the future. In addition, continuing dupilumab treatment despite development of this adverse effect is an essential consideration, as this reaction may respond favorably to local treatment.

CONFLICT OF INTEREST

The authors declare no potential conflict of interests.

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