Efficacy of Dupilumab in Patients with Atopic Dermatitis and Alopecia Areata: A Case Series

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Abstract

Alopecia areata is a non-scarring immune-mediated alopecia, more common in patients affected by atopic dermatitis, in which a pathogenetic role of Th2 cells has been suggested. In Italy, at present, patients suffering from severe atopic dermatitis (Erythema Area and Severity Index, EASI, score ≥ 24), nonresponding or non-eligible to cyclosporine-A, are successfully treated with dupilumab, a monoclonal antibody blocking interleukin-4 and interleukin-13 signalling pathway. Herein we report the cases of four patients, three adults and one child, affected by both atopic dermatitis and alopecia areata, who were treated with dupilumab.

Two adult patients achieved a complete, or almost complete, and sustained response in their alopecia areata when treated with dupilumab. The paediatric patient experienced a temporary improvement, while the fourth patient did not respond to treatment.

Our findings are consistent with existing literature that suggests a dysregulation of the Th2 axis, which includes interleukin-4 and interleukin-13, playing a role in the development of alopecia areata. However, further research is needed to confirm the efficacy of dupilumab in treating alopecia areata.

Keywords: Dupilumab; Alopecia areata; Atopic eczema

Key summary points

Dupilumab, a monoclonal antibody used for the treatment of atopic eczema, could also represent a valuable option for patients affected by alopecia areata. Contrasting results has emerged from different papers in literature. Our case-series describe a significant improvement of both diseases in two adult patients and a transient improvement of alopecia areata in an atopic paediatric patient while on dupilumab therapy.

Introduction

Alopecia Areata (AA) is an autoimmune condition characterized by patchy hair loss, where the body’s immune system mistakenly attacks the hair follicles. Atopic Dermatitis (AD), also known as atopic eczema, is a chronic inflammatory skin condition. One of the largest association studies conducted on patients suffering from AA found an association with several dermatological conditions including AD (OR 2.24, 95% CI 1.95-2.58) [1]. While the exact relationship between the two conditions is not fully understood, it is believed that they may share common
immunological mechanisms. One proposed mechanism involves the role of Th2 cells, which are a type of T-helper cell involved in the immune response; Th2 cells are known to be predominant in atopic dermatitis and may also play a role in the development of AA [2-5].

Dupilumab is a human monoclonal antibody that inhibits the α subunit of the interleukin (IL)-4 receptor and thus blocks the co-transduction of IL-4 and IL-13 signals, resulting in a reduced immune Th2 response. Dupilumab is highly effective in AD and has a good safety profile [6]. In Italy, for adult patients affected by a severe AD (Erythema Area and Severity Index, EASI, score ≥ 24), dupilumab is reimbursed by the National Health Service (NHS) when treatment with cyclosporine-A is contraindicated, ineffective, or not tolerated (Determina n. DG/133/2018, GU n.208 del 7-9-2018). In children and adolescents, aged 6 to 17 years, dupilumab reimbursement by the Italian NHS occurs in the case of a severe AD (EASI score ≥ 24) or one of the following criteria: localization in visible and/or sensitive areas, a NRS (Numerical Rating Scale) pruritus score ≥ 7, a DLQI (Dermatology Life Quality Index) score ≥ 10 (Determina n. DG/1203/2020 GU n. 305 del 09-12-2020, Determina n.115/2022, GU n.42 del 19-02-2022). Several studies and case reports have explored the use of dupilumab in AA, particularly in patients with concomitant AD or who have not responded to traditional AA treatments. The results have been mixed, with some studies reporting positive outcomes and others showing limited or no significant improvement.

Case-Reports

Herein we report the cases of four patients, three adults and one child, affected by both a severe AD and AA who were treated with dupilumab. Table 1 provides a summary of patients’ medical history. All patients were affected by a severe form of AD (EASI >24) not manageable with the topical use of moisturizers and corticosteroids (CCS; mometasone furoate 1 mg/g cream, 1 application per day for at least 3 weeks). For the severity of the AD two adult patients required courses of oral (CCS) therapy with prednisone at a starting dosage of 25 mg daily. One adult patient underwent a narrow-band-UVB (nb-UVB) phototherapy course (2 exposures per week for 5 months) without reaching a significant improvement (final EASI 15, final VAS pruritus 7/10). Two adult patients were non-eligible to systemic treatment with cyclosporine-A due respectively to recurrent herpetic infections (more than 6 episodes in a year) and hypertension; the remaining adult patient obtained an inadequate disease control with a 6-month course of therapy with cyclosporine-A.

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Female</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Age (years)</td>
<td>39</td>
<td>47</td>
<td>23</td>
<td>11</td>
</tr>
<tr>
<td>Previous therapy for AD</td>
<td>Moisturizers, topical and oral CCS</td>
<td>Moisturizers, topical and oral CCS nb-UVB</td>
<td>Moisturizers, topical CCS, cyclosporine-A</td>
<td>Moisturizers, topical CCS</td>
</tr>
<tr>
<td>Previous therapy for AA</td>
<td>Minoxidil 5%, topical and oral CCS</td>
<td>Minoxidil 5%, topical and oral CCS</td>
<td>Topical and intralesional CCS</td>
<td>Topical CCS</td>
</tr>
<tr>
<td>AD severity at baseline</td>
<td>Severe EASI 26 VAS pruritus 10/10</td>
<td>Severe EASI 29.3 VAS pruritus 9/10</td>
<td>Severe EASI 26 VAS pruritus 10/10</td>
<td>Severe EASI 21.5 VAS pruritus 8/10</td>
</tr>
<tr>
<td>AA severity at baseline</td>
<td>Whole scalp, eyebrows SALT 85%</td>
<td>Whole scalp SALT 100%</td>
<td>AA universalis SALT 100%</td>
<td>Vertex and eyebrows SALT 40%</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Asthma, allergic rhinoconjunctivitis, recurrent herpetic infections</td>
<td>Asthma, allergic rhinoconjunctivitis, polyallergy, autoimmune gastritis, arterial hypertension</td>
<td>Asthma, allergic rhinoconjunctivitis</td>
<td>None</td>
</tr>
<tr>
<td>Laboratory</td>
<td>Total eosinophilic count 0.8*10^9/L total IgE 352 kU/L</td>
<td>Total eosinophilic count 0.6*10^9/L total IgE 1331 kU/L</td>
<td>Total IgE 73 kU/L</td>
<td>NR</td>
</tr>
</tbody>
</table>

Table 1: patients characteristics. AD – Atopic Dermatitis; AA – Alopecia Areata; CCS – Corticosteroids; EASI – Eczema Area and Severity Index; nb-UVB – narrow band-UVB; SALT – Severity of Alopecia Tool; VAS – Visual Analogue Scale; NR – Not Reported.

<table>
<thead>
<tr>
<th>AD response at week 16</th>
<th>Complete</th>
<th>Partial (EASI 3)</th>
<th>Complete</th>
<th>Complete</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA response at week 16</td>
<td>Partial</td>
<td>Partial</td>
<td>No response</td>
<td>Partial</td>
</tr>
</tbody>
</table>

All patients were simultaneously affected by AA and failed to obtain a long-term remission of the disease with conventional therapies including, for adult patients, topical minoxidil 5% (2 mL die for 12 months), clobetasole propionate 0.05% foam for six months, subcutaneous injections of triamcinolone acetonide 40 mg/1mL (1 injection every 2 weeks for 3 months) and courses of oral prednisone at a starting dosage of 25 mg die. The paediatric did not respond to topical CCS (clobetasole propionate 0.05% foam for six months). In one adult patient and in the paediatric patient AA also involved the eyebrows. One adult patient was suffering from AA universalis.

Subcutaneous dupilumab was started for the severe AD in all adult patients with an initial dose of 600 mg and, according to the treatment plan, following 300-mg dose every other week. The paediatric patient received an initial dose of dupilumab 300 mg followed by another dose after 15 days; a maintenance dosage of dupilumab 300 mg every 4 weeks was established. All patients achieved a quick remission of AD after a mean of 16 weeks (median EASI 3; min 0, max 6). At this time point two adult patients showed an abundant development of vellus hair on trichoscopy of the scalp. In the subsequent examinations the regrowth of normal terminal hair was seen and after a mean of 12 months of treatment hair almost returned to normality (SALT 10%) (Figure 1). However, in one patient, due to a severe dupilumab-induced blepharoconjunctivitis, the drug was discontinued. Two months after dupilumab cessation a severe relapse of both AA (SALT 100%) and AD (EASI 15) occurred and therefore the patient was prescribed upadacitinib cp 15 mg per day obtaining a complete remission of the AD (EASI 0) at 4-month follow up, but only a partial improvement of the AA (SALT 80%) at 8-month follow up (Figure 2).

Figure 1: A) Clinical images of a 39-year-old female patient at baseline evaluation showing a severe AA of the scalp (SALT 85%). Note the painted eyebrows. B) Baseline trichoscopy images showing empty follicles and yellow dots. C and D) Clinical images of the same patient after 8-months of dupilumab therapy for a concomitant severe AD. A diffuse hair and eyebrows regrowth are shown (SALT 10%). E) Trichoscopy images taken 8-months after starting dupilumab.
the efficacy of dupilumab for the treatment of AA. Studies have shown significant hair growth in some patients (n=23), and no change in others (n=3). One case reported hair loss 8 weeks after dupilumab was discontinued [11]. Despite the promising results of dupilumab for the treatment of AA, 1 retrospective case study, 3 case series and 12 case reports discuss an AA-like hair loss in patients receiving treatment for AD.

Our small case-series reflects what is described in literature: we report the cases of four patients with both AA and AD who were prescribed with dupilumab. Two adult patients achieved a complete and persistent response in AD and AA while taking dupilumab, one paediatric patient had a transient improvement on AA and another adult patient had no improvement.

Aspects that could determine the effectiveness of dupilumab in AA and that should be further investigated are the duration of AA, the extent of the alopecia, a family history of atopy and biomarkers such as total IgE. In a phase 2a randomized clinical trial of dupilumab for alopecia areata adult patients demonstrated that responders were more likely to have personal or familial atopy and/or high serum total IgE levels (≥200 IU/ml) as compared to non-responders [12].

To date, only few published case reports describe cases of children affected by both AD and AA treated with dupilumab. Investigating the role of dupilumab in these patients could be particularly useful since it has a reassuring safety profile. Moreover, upadacitinib, a JAK inhibitor approved for severe AD that has shown promising results also on AA, is not approved for use in children under the age of 12 [13-14].

Conclusions

Our case-series describe a significant improvement of both AD and AA in two adult patients and a transient improvement of AA in an atopic paediatric patient on dupilumab therapy. We also report the case of an adult patient who did not achieve any improvement on AA while taking dupilumab for a severe AD. Our results suggest that dupilumab may be effective for AA in patients with severe AD. However, as outlined by a recent systematic review [10], contrasting results has emerged from different papers, with some showing a good outcome and others even pointing out how dupilumab may be causing hair loss. Therefore, further studies with large samples are needed to clarify the role of dupilumab in AA, especially in paediatric populations.

Disclosures

Authors declare no competing interests regarding this article. All subjects provided informed consent to publication.
References


