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CASE REPORT

Complete hair regrowth in a young male with severe atopic dermatitis and alopecia areata after dupilumab: probably more than a coincidence

Repovoamento completo num adulto jovem com dermatite atópica grave e alopecia areata após dupilumab: provavelmente mais do que coincidência

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Abstract

We report the case of a 29-year-old male patient who has suffered from severe atopic dermatitis (AD) since early childhood and presented with a 6-month evolution of patchy hair loss in the temporal and occipital regions, clinically suggestive of alopecia areata (AA), which was confirmed by scalp biopsy. The patient started therapy for atopic dermatitis with the monoclonal antibody dupilumab, with a substantial response regarding atopic dermatitis, and with renewed hair growth on the scalp. Dupilumab blocks the α-subunit of the interleukin 4 receptor, interrupting the signaling cascade of IL-4 and IL-13 and thus leading to a reduced Th2 immune response. Some controversy exists regarding dupilumab and AA, with some reports describing improvement after starting this drug while others showing patients with dupilumab-induced alopecia. The patient demonstrated dramatic improvement in both AD and AA early on and tolerated the drug without significant side effects. His quality of life was significantly improved. Patient selection could play a crucial role in the future, and the predictors of a good response are currently being identified so the responders with severe atopic dermatitis and alopecia areata could benefit from dupilumab.

Keywords: Alopecia areata. Dupilumab. Atopic dermatitis.

Resumo

Relatamos o caso de um doente do sexo masculino de 29 anos com dermatite atópica (DA) grave desde a infância com um quadro com 6 meses de evolução de perda de cabelo em padrão irregular nas regiões temporal e occipital clinicamente compatível com alopecia areata (AA), o que foi corroborado com biópsia do couro cabeludo. O doente iniciou terapêutica com o anticorpo monoclonal dupilumab, com melhoria substancial da dermatite atópica e com rápido repovoamento do couro cabeludo. O dupilumab bloqueia a subunidade α do receptor da interleucina 4, interrompendo a cascata de sinalização da IL-4 e IL-13 e reduz assim a resposta imune Th2. Existe alguma controvérsia em relação ao dupilumab e à AA, com alguns estudos a descrever melhoria após o início do fármaco, enquanto outros relatam doentes com alopecia induzida por dupilumab. O doente

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demonstrou melhoria dramática quer da DA, quer da AA precocemente e tolerou o fármaco sem efeitos colaterais significativos. A qualidade de vida melhorou significativamente. A seleção de doentes poderá desempenhar um papel crucial no futuro, com os preditores de uma boa resposta a serem identificados para selecionar os potenciais doentes com dermatite atópica grave e alopecia areata com a melhor resposta ao tratamento.

***Palavras-chave*:** Alopecia Areata. Dupilumab. Dermatite Atópica.

Introduction

Alopecia Areata (AA) is an autoimmune disorder characterized by nonscarring hair loss with preservation of the hair follicle, affecting up to 2% of the general population and imposing a significant psychological impact on affected patients[1].

AA can present in multiple patterns, and its severity may range from episodes of well-defined patchy hair loss on the scalp to the more serious and complete scalp (alopecia totalis) and total body hair loss (alopecia universalis)[2].

The theory of loss of the immune privilege of the hair follicle is thought to play a crucial role in AA[3]. The presumed target antigen is yet to be defined. The succeeding loss of hair follicle immune privilege results in the recognition of hair follicle autoantigens by autoreactive $CD8^+$ T cells[4]. Patients with AA have a constellation of potentially associated autoimmune conditions and an increased risk of Atopic Dermatitis (AD)[3].

Common treatment options for extensive AA, where intralesional and topical treatments are often of restricted applicability, include systemic immunosuppressants like methotrexate and cyclosporin, which generally provide temporary responses and are unsuitable for long time use[5]. Thus, there is a great demand for new, specific treatments for long-term disease control in moderate-to-severe AA.

Indeed, recent evidence suggests that Dupilumab, a monoclonal antibody directed against the IL-4 receptor α subunit blocking both IL-4 and IL-13 signaling and currently approved for the treatment of atopic dermatitis, could be of some benefit in AA[6].

Baricitinib, a Janus kinase inhibitor, has been approved for severe AA and other drugs from this class are presently undergoing clinical trials with positive preliminary results[7].

Cases have been reported of the improvement of AA in patients with concomitant AD receiving treatment with dupilumab[8].

The effect of dupilumab in AA has been postulated to be the inhibition of Th2 pathway activation found in AA scalp lesions[9]. Nevertheless, dupilumab has also been associated with AA both in patients with preexisting AA and those without a prior diagnosis of AA[10].

Case synopsis

A 29-year-old man was evaluated due to uncontrolled AD. He had a history of recurrent flares of AD since childhood with worsening in the last 2 years. He also had a 6-month history of round patchy hair loss.

He had AD from the age of 3, with severe itching, sleep deprivation, and a great impact on his quality of life and was on an almost persistent use of topical corticosteroids and calcineurin inhibitors and occasional courses of systemic therapies with prednisolone as well as cyclosporin with limited and transient benefit. He reported asthma in childhood with spontaneous improvement and no current need for therapy.

Of relevance, he also had an episode of eczema herpeticum and herpetic keratoconjunctivitis treated with intravenous acyclovir a couple of weeks prior to the observation.

On physical examination, multiple erythematous papules and plaques, some of which were severely excoriated by scratching, were found on the entire skin including the face, cervical region, flexures of the forearm, and knees. EASI score was 14,6. He also had several patches of alopecia on occipital, temporal, and parietal regions, with scaling and erythema (Fig. 1). The eyebrows, eyelashes, and body hair was spared.

Laboratory tests were normal (hemogram with differential blood count, kidney, liver and thyroid function, and electrolytes) except for increased serum IgE levels (3055.3 IU/mL). Trichoscopy showed yellow and black dots and a perifollicular scale. Two 4 mm punch biopsies were performed on the scalp, showing dermis with adnexal rarefaction, presence of a sebaceous component, and fibrosis with a mild lymphocytic infiltrate and "stela" like structures, favoring the diagnosis of alopecia areata.

He was started on dupilumab with an initial dose of 600 mg followed by 300 mg every 2 weeks.

The patient was observed to evaluate the response 16 weeks after the first dose of dupilumab, with a

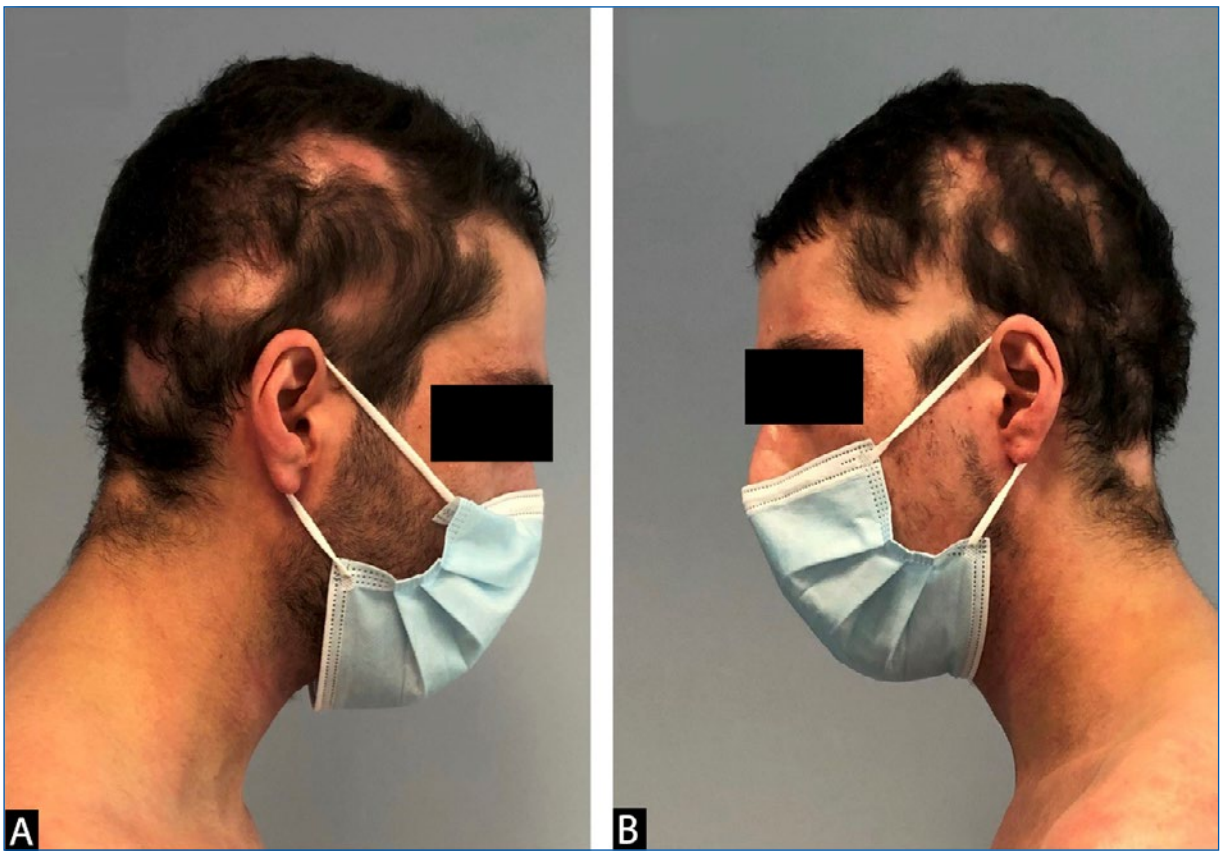

Figure 1. A and B: patches of alopecia on occipital, temporal, and parietal regions, with scaling and erythema.

dramatic improvement regarding atopic dermatitis with an EASI drop close to 0 and a resolution of the itching, a better sleep pattern and no need for any topical therapy except emollients. He also had full hair regrowth in the areas previously affected by AA (Fig. 2).

Except for slight conjunctivitis, which was successfully treated with artificial tears, the patient had no side effects and so far has tolerated the medication extremely well.

Discussion

Patients with AA show elevated levels of type 2 cytokines suggesting that Th2 axis suppression may be a therapeutic target for AA[9]. As dupilumab-induced IL-4 inhibition results in a decrease in inflammatory mediators, it likely leads to concomitant improvement of both AA and AD[11].

According to previous reports, hair regrowth with dupilumab usually begins between 3 and 6 months of therapy, although it may begin earlier[12].

However, the relationship between dupilumab and alopecia areata remains controversial as some patients experience improvement after starting treatment while others develop dupilumab-induced alopecia[13] with some studies suggesting that Th2 inhibition may amplify alternate pathways such as Th1 and Th17 resulting in hair loss[14]. Moreover, alopecia associated with dupilumab tends to follow an androgenetic pattern and usually has an eczematous pattern upon histopathological examination[15]. It is unclear whether dupilumab induces true AA or a form of drug-induced alopecia.

Janus Kinase Inhibitors have shown efficacy for moderate-to-severe AA[16]. In this case, baricitinib could have been an option due to the coexistence of AA and AD. However, due to the recent eczema herpeticum, we opted for dupilumab due to its safety and were extremely pleased by the effect on hair regrowth.

However, we should highlight that the temporal relationship between dupilumab use and AA hair regrowth does not ensure causality, as there may be

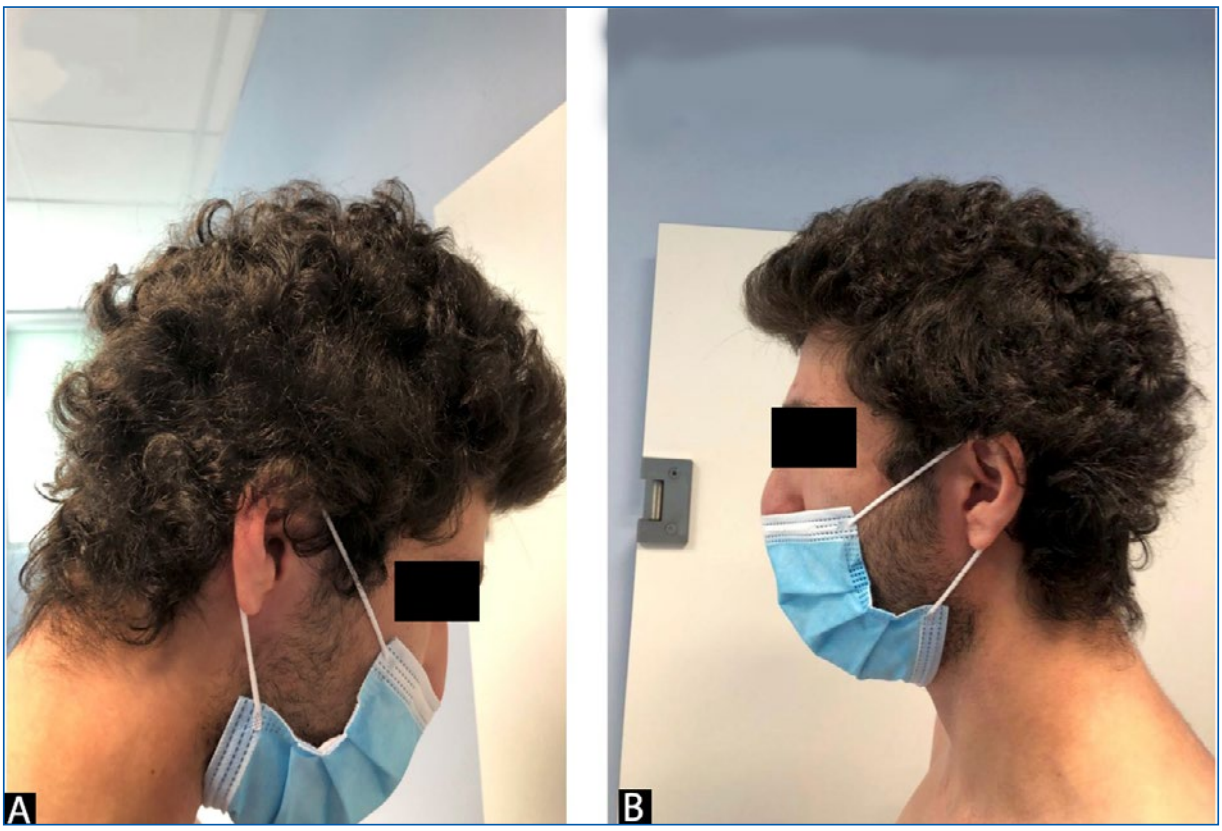

Figure 2. A and B: hair regrowth after 16 weeks of treatment with dupilumab.

spontaneous AA improvement. Therefore, we cannot attribute this fast improvement to dupilumab with certainty.

A study using the VigiBase, a real-world pharmacovigilance database concluded that hair disorders corresponded to 2.2% of total dupilumab adverse events. This study concluded that dupilumab was associated with both hair growth and loss and overall, the paradoxical results of dupilumab in hair disorders might be caused by complex disease factors, such as IgE and IL-4 levels and the complexity of AA pathogenesis[14].

A clinical trial has recently demonstrated the pathogenic role of the Th2 axis in AA and the efficacy of dupilumab in moderate-to-severe AA[17]. Furthermore, this trial showed that patients with IgE ≥ 200 IU/mL had an odds ratio of 8.1 to respond to dupilumab treatment compared to those with low baseline IgE, suggesting that IgE may be a tool for patient selection for dupilumab treatment, a new concept in AA management. A possible explanation for these findings may be that increased levels of serum IgE are indicative of Th2 -associated inflammation in the hair follicle, which may respond better to Th2-targeting approaches[17].

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None to declare.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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