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Long-Term Efficacy of Dupilumab in Alopecia Areata

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Data Interpretation D
Manuscript Preparation E
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Patient: Male, 16-year-old
Final Diagnosis: Alopecia areata
Symptoms: Scalp hair loss
Medication: —
Clinical Procedure: —
Specialty: Dermatology

Objective: Unusual or unexpected effect of treatment

Background: Dupilumab is a relatively new immune-modulating drug that has transformed the way clinicians treat common immunologic conditions, including atopic dermatitis, asthma, and chronic rhinosinusitis with nasal polyposis. Blocking signaling molecules involved within the Th2 immune response, dupilumab is a proven effective treatment for moderate to severe atopic dermatitis – a condition whose disease pathogenesis is heavily linked to the dysregulation of this immunologic pathway. Interestingly, dupilumab has found broader clinical utility, showing efficacy in treating other distinct dermatologic diseases, including alopecia areata.

Case Report: A 16-year-old White male with a past medical history of moderate atopic dermatitis presented to our clinic with complete scalp hair, eyebrow, and eyelash loss. At this time, the patient was given a clinical diagnosis of alopecia totalis. Understanding that dupilumab has been previously used for treatment in adults of this specific autoimmune condition, we started this adolescent patient on dupilumab to concomitantly treat his atopic dermatitis and alopecia areata. The patient gradually experienced complete regrowth of his hair and almost complete resolution of his atopic dermatitis. Three years after starting dupilumab, the patient remains without signs of alopecia totalis.

Conclusions: This case report demonstrates the long-term efficacy of dupilumab use in alopecia areata. More investigation is required to understand dupilumab's broadening clinical indications. Additionally, this case highlights the complex relationship between dysregulation of the Th2 response and autoimmunity. Crosstalk between immune pathways within the disease spectrum of alopecia areata may explain why dupilumab has been reported to both treat and exacerbate alopecia areata.

Keywords: Dupilumab • Alopecia Areata • Autoimmunity

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/936488

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Background

Alopecia areata (AA) is an autoimmune disorder causing hair loss. A subtype of AA is alopecia totalis, in which patients experience complete hair loss of the scalp, often accompanied by loss of eyebrows and eyelashes [1]. Traditional therapies for AA include topical and intralesional corticosteroids, topical immunotherapy, and topical minoxidil for localized disease; systemic immunosuppressive therapies, including cyclosporine, systemic corticosteroids, and JAK/STAT inhibitors have been utilized in widespread disease. Treatment success has been shown to be highly variable and individualistic, with high rates of recurrence after cessation of systemic therapy.

Within the last several years, literature reviews have shown that dupilumab, a monoclonal antibody directed against the IL-4 receptor alpha subunit, can be efficacious in the treatment of alopecia areata [2-4]. This case report highlights how dupilumab was used to treat alopecia totalis in an adolescent White male with concomitant moderate atopic dermatitis. Although use of dupilumab in this scenario is not novel, our case report remains unique in demonstrating long-term (~3-year) efficacy of dupilumab in treating both atopic dermatitis and AA.

Case Report

Our patient, a 16-year-old White male, presented to his primary care physician after noticing a 5-cm patch of alopecia on his occiput. Suspecting tinea capitis, his physician prescribed topical terbinafine cream. With this regimen the patient did not show clinical improvement. In fact, within the next several months, the patient had expansion of the initial lesion as well as several other patches of hair loss on his scalp. Within 8 months of initial presentation, the patient had complete loss of his scalp hair, eyebrows, and eyelashes as seen in **Figure 1**.

At this time, the patient presented to our dermatology clinic and was given the clinical diagnosis of alopecia totalis. Although dermatoscopic techniques could have confirmed the diagnosis, they were not used, as the disease process was evident from the patient's presenting symptoms. This was the patient's first occurrence of alopecia areata, its onset being acute in nature. The patient also had a past medical history of atopic dermatitis, first diagnosed in childhood. The patient's atopic dermatitis was inadequately controlled with topical corticosteroids, presenting with several erythematous eczematous patches distributed primarily on the arms and trunk. Other significant past medical history includes a type I allergy to eggs as well as asthma that was well controlled with montelukast. He had no family history of atopy or alopecia areata.

Figure 1. Patient showing complete hair loss of scalp, eyebrows, and eyelashes at baseline.

Due to the patient having widespread alopecia totalis and given the concomitant diagnosis of moderate uncontrolled atopic dermatitis, he was started on dupilumab along with topical corticosteroid therapy. The patient received a loading dose of 600 mg dupilumab and then 300 mg injections every 2 weeks. Within the next several months of starting this new regimen, the patient would experience gradual regrowth of his scalp hair, as seen in **Figure 2A**. Of note, the patient's atopic dermatitis substantially improved while on this regimen as well. When initially started on dupilumab, the patient had a BSA of 25% and an IGA of 3, moderate. He demonstrated a BSA of 1% and an IGA of 1, almost clear, after 6 months of therapy.

Within 8 months of starting dupilumab, the patient had almost complete regrowth of his scalp hair, as seen in **Figure 2B**. After almost 3 years on this regimen, the patient continues to see no evidence of recurrence of alopecia areata, as shown in **Figure 2C**.

Discussion

Dupilumab targets Th2 mediated cytokine signaling through blockade of IL-4 and IL-13, making it effective for the treatment of certain autoimmune disorders implicated in the pathway. The drug has been FDA approved for moderate-to-severe atopic dermatitis, eosinophilic or oral steroid dependent asthma, and chronic rhinosinusitis with nasal polyposis [5]. Several studies have shown the long-term efficacy of dupilumab in the context of atopic dermatitis and asthma [6,7]. However, literature review yields no such findings for treatment of acute

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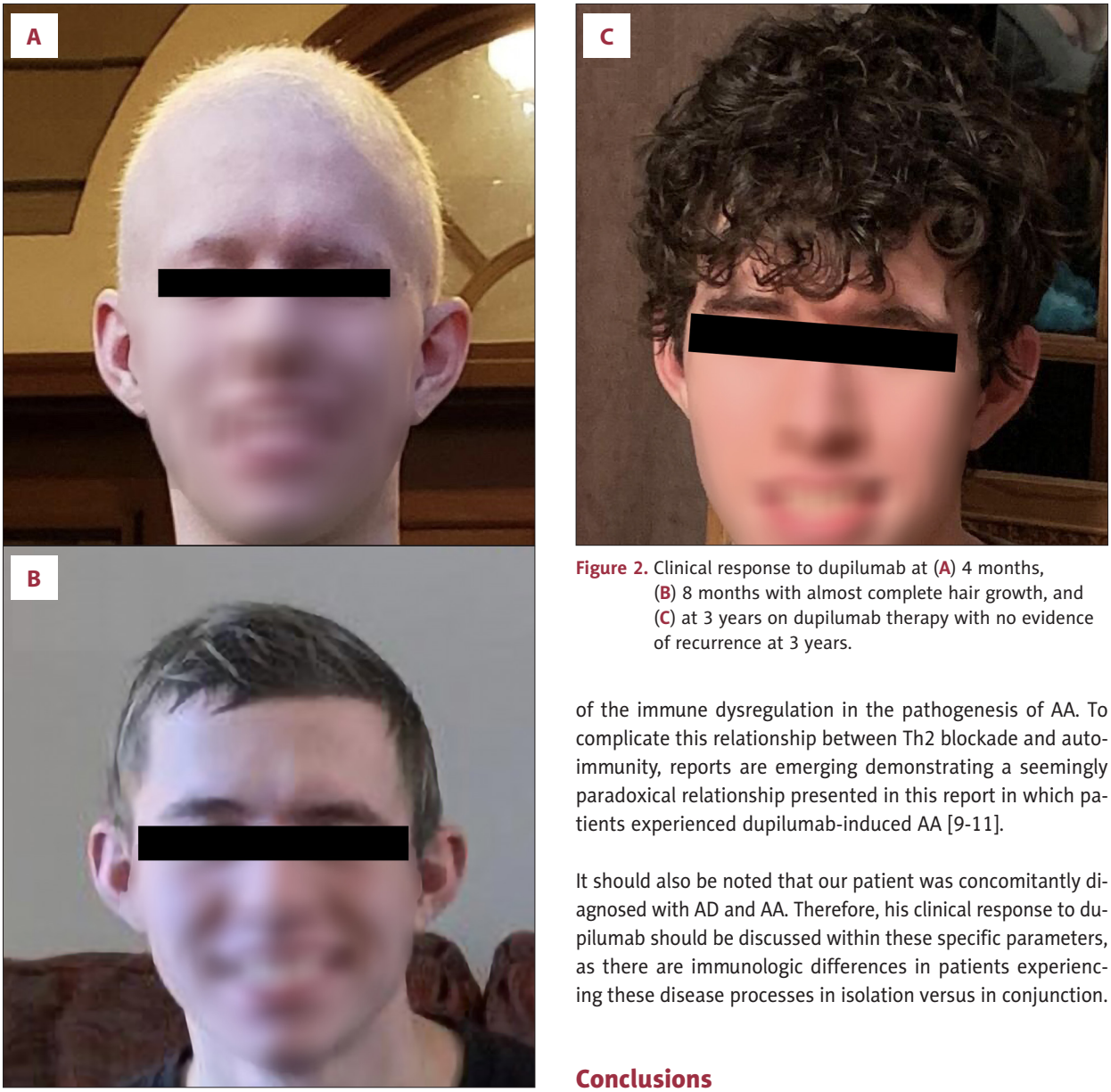

Figure 2. Clinical response to dupilumab at (**A**) 4 months, (**B**) 8 months with almost complete hair growth, and (**C**) at 3 years on dupilumab therapy with no evidence of recurrence at 3 years.

alopecia areata, likely because dupilumab has not yet received FDA approval for this specific disease process.

The pathogenesis of AA and other autoimmune conditions has been classically described as Th1/Th17-mediated. However, key studies have shown that this may be an oversimplification, and that autoimmune conditions can also involve the Th2 pathway [8]. Furthermore, more complex crosstalk between the Th1, 2, and 17 pathways seem to be at play. The leading hypothesis for this crosstalk proposes that blockade of the Th2 response – as seen with dupilumab – can dysregulate Th1/Th17 responses, causing a cytokine shift. Our case report, alongside similar reports showing dupilumab's success with treating AA, suggests that Th2 overactivity could be part of the immune dysregulation in the pathogenesis of AA. To complicate this relationship between Th2 blockade and autoimmunity, reports are emerging demonstrating a seemingly paradoxical relationship presented in this report in which patients experienced dupilumab-induced AA [9-11].

It should also be noted that our patient was concomitantly diagnosed with AD and AA. Therefore, his clinical response to dupilumab should be discussed within these specific parameters, as there are immunologic differences in patients experiencing these disease processes in isolation versus in conjunction.

Conclusions

The relationship between Th2 blockade and autoimmunity appears to be a spectrum within the specific disorder of AA. Based on the above hypothesis, the variables that dictate whether Th2 blockade upregulates or downregulates the Th1/Th17 response – and thus whether dupilumab induces or treats AA – are unknown at this time. More investigation is required to understand the complexity of the immune response in this regard.

This case report highlights the long-term efficacy of dupilumab in acute alopecia areata spanning 3 years. These findings may suggest that broadening the scope of dupilumab treatment is justified and fruitful. More specifically, this treatment may be considered when treating autoimmune conditions in patients with concomitant atopic dermatitis. Clearly, more

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clinical research is required to understand the value of dupilumab in the setting of other disease processes that involve the T-helper responses.

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