

CLINICAL COMMENTARY

Dupilumab for alopecia areata treatment: A double-edged sword?

Peng Jin MD¹ | Li Wei BS² | Qinqin Zhang MSc¹ | Tingting Gao BS³ |
Jianxue Bai MSc⁴ | Liang Dong MD⁵ | Lili Zhi MSc³ 

¹Department of Otolaryngology, The Second Hospital, Cheeloo College of Medicine, Shandong University, Jinan, China

²Department of Respiratory, Linyi People's Hospital, Linyi, China

³Department of Allergy, Shandong Institute of Respiratory Diseases, Shandong Provincial Qianfoshan Hospital, The First Affiliated Hospital of Shandong First Medical University, Jinan, China

⁴Department of Dermatology, Traditional Chinese Medicine Hospital of Huantai, Zibo, China

⁵Department of Respiratory, Shandong Institute of Respiratory Diseases, Shandong Provincial Qianfoshan Hospital, The First Affiliated Hospital of Shandong First Medical University, Shandong University, Jinan, China

Correspondence

Lili Zhi, Department of Allergy, Shandong Provincial Qianfoshan Hospital, The First Affiliated Hospital of Shandong First Medical University, Shandong Institute of Respiratory Diseases, No. 16766, Jingshi Road, Jinan, Shandong Province 250013, China.

Email: qfsyallergy@163.com

Funding information

This work was supported by the grants from National Natural Science Foundation of China (81800885)

Abstract

Alopecia areata (AA), which is a common and inflammatory hair loss and one of the most frequent dermatological conditions with higher incidence worldwide, the complex interplay involved multiple factors was contributed to the pathogenesis that consists of immune privilege losing and destruction with autoimmune-mediated in hair follicle also the abnormal regulation of inflammatory pathways was highlighted, although it was remained unclear to date. (J Am Acad Dermatol, 78, 2018, 1) Some treatment options for AA were proposed with great advances in recent years, but the options and efficacy were limited, such as platelet-rich plasma, JAK-STAT inhibitor, PDE4 inhibitor, and others, also the good response with regrow hair of cytokine-targeted therapy like dupilumab, ustekinumab was shown. (Clin Exp Med, 21, 2021, 215; Drugs, 80, 2020, 635) Here, we present a case with onset of AA following dupilumab treatment, the chronological relationship between the AA onset and dupilumab use should be known and emphasized.

KEYWORDS

alopecia areata, biologics, dupilumab, inflammation

1 | CASE REPORT

A 63-year-old woman with a long-time history of poor-controlled asthma that clinically presented as recurrent and reversible severe cough and wheezing that seriously affecting the quality of life, also the poor response to inhaled medications. Any systemic symptoms such as fever, joint pain, photosensitive symptom, and similar family history were denied. The pulmonary function test revealed moderate to severe obstructive abnormal airway function. Upon the further evaluation of whatever the laboratory and chest

imaging, no positive findings were found except that the eosinophil count increased slightly ($0.6 \times 10^9/L$, $0.02-0.52 \times 10^9/L$ was normal range), which included complete blood count, total immunoglobulin E (IgE), specific IgE, antineutrophil cytoplasmic antibody (ANCA), antinuclear antibody (ANA), rheumatoid factor, inflammatory cytokines (interleukin-6, 8, 10, and tumor necrosis factor- α), galactomannan antigen, 1-3- β -D-glucan, and serum tumor markers. The patient refused to receive glucocorticoid treatment out of fear of glucocorticoid use and its adverse reaction. A treatment option of subcutaneous injection dupilumab with an initial dose of 600 mg was

performed, the respiratory symptoms improved significantly also denied some serious adverse reactions but complained that the hair fell off more than usual during the 1-week follow-up after the injection. According to the treatment plan, the subcutaneous injection dupilumab with 300-mg dose was again given after 2 weeks, the patient complicated with significant hair loss developed within 3 days after injection and the dermatologist consulted was taken. Upon physical examination, diffuse and multiple non-scarring alopecia patches on the scalp were shown (Figure 1A,B), hair pull test and trichoscopy examination for further detection, clinical and trichoscopic findings were consisted of a diagnosis of alopecia areata (AA) in dermatology consulted. The patient refused topical glucocorticoid and topical minoxidil was recommended. Since the onset of AA following dupilumab treatment, the chronological relationship was considered, the patient was asked to stop dupilumab treatment and continue to receive inhaled medication treatment. After using minoxidil for 6 months, the hair was regenerated and returned to normal, there was no evidence of AA recurrence in one-year follow-up (Figure 1C).

2 | DISCUSSION

With the development of biologics in recent years, among them, the biologics using on allergic disease was proposed and widespread using with positive effectiveness and safety. Th2 cytokines included interleukin (IL)-4 and IL-13 also the heterodimeric IL-4 receptor (IL-4R) complexes that they interact with play a critical role in the link and pathogenesis of allergic diseases. Dupilumab as a fully human anti-IL-4 receptor α -monoclonal antibody that blocks both IL-4 and IL-13 signaling, which is an effective and safe option for allergic diseases like asthma, atopic dermatitis, and others treatment.^{1,2} Besides that, some case series also the randomized clinical trial revealed and indicated the effectiveness on hair regrowing with dupilumab treatment and considered as a potential treatment option for AA.^{3,4} Alopecia areata which is an autoimmune, multifactorial dermatological disease and one of non-scarring hair loss, it can lead to scalp or/and around the body with small patches of baldness.⁵ In fact, both the pathogenesis and pathobiology of AA

was remained unclear and elusive, multiple factors can contribute to it like genetic, environment factors, but the common theory preferred immunological mechanism subsequent to triggering events that presented as the collapse of the immune privilege of the hair follicle.⁶⁻⁸ The type 1 inflammatory disease has been recognized in AA, but recent evidence showed roles of type 2- and Th17-associated mediators in AA pathogenesis, the successful treatment with dupilumab in patients with AA confirmed and indicated the possible pathogenic role of the Th2 axis and Th2 targeting in patients with AA.^{4,8} Although the Th2 axis was suggested and indicated it can contribute to AA pathogenesis, Th1 axis was still played a critical role in it and should be also highlighted. Our case presented an asthma patient with onset of AA following the dupilumab treatment, this chronological relationship suggests an association between AA onset and dupilumab treatment, the Th1/Th2 axis imbalance maybe contributed to it, dupilumab as a Th2 targeting biologics result downregulate the Th2 pathway while the amplification of the Th1 pathway was probably presented and then mediate even directly promote the onset of AA. Onset of AA following omalizumab has been described in the past, interestingly, the similar pathogenesis of onset of AA following omalizumab treatment was suggested also associated with imbalance of Th1 / Th2 axis.^{9,10}

In conclusion, this chronological relationship suggests an association between AA onset and dupilumab treatment; however, the current evidence shows that dupilumab is an effective and safe option for AA treatment that based on the Th2 axis and type 2-associated mediators contributed to AA pathogenesis. Although the Th2 axis was suggested and indicated it can contribute to AA pathogenesis, Th1 axis was still played a critical role in it and should be also highlighted. Whether AA should be considered as a potential adverse skin reaction of dupilumab is debatable, but dermatologists should understand and pay attention to the chronological relationship between AA onset and dupilumab use. Due to the complex pathogenesis of AA, the clinical trial results of high-level evidence of dupilumab in the treatment of AA are worth looking forward to. Shortly, based on the complex inflammatory driving mechanism, dupilumab should be considered as a double-edged sword in AA treatment.

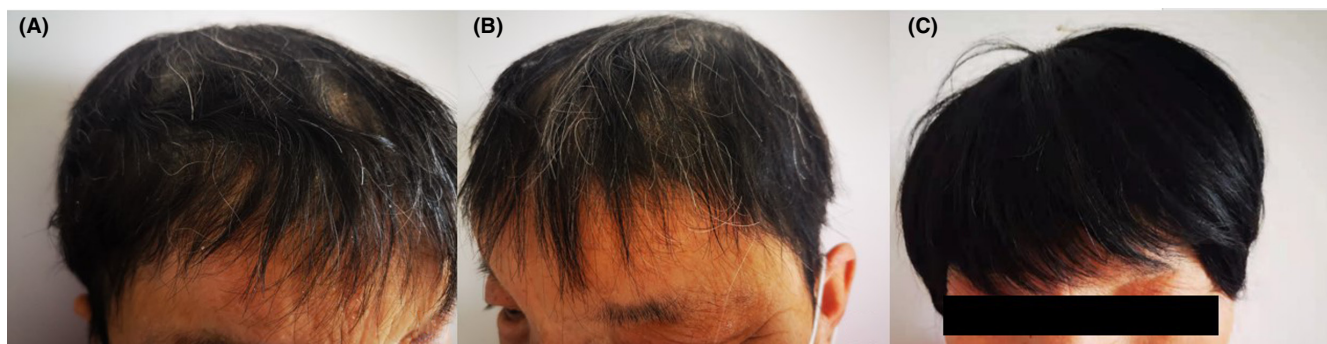


FIGURE 1 (A and B) Upon physical examination, diffuse and multiple non-scarring alopecia patches on the scalp were shown. (C) After using minoxidil for 6 months, the hair was regenerated and returned to normal, there was no evidence of AA recurrence in one-year follow-up

AUTHOR CONTRIBUTIONS

Lili Zhi and Liang Dong involved in conceptualization, administration, and validation. Peng Jin, Li Wei, Qinqin Zhang, Tingting Gao, and Jianxue Bai involved in data collection. Peng Jin and Qinqin Zhang wrote the original draft. Peng Jin, Qinqin Zhang, Lili Zhi, and Liang Dong reviewed and edited the draft. All authors approved the final version.

ACKNOWLEDGEMENT

None.

CONFLICT OF INTEREST

None.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable—no new data are generated, or the article describes entirely theoretical research.

ETHICAL APPROVAL

Not applicable.

INFORMED CONSENT

The written informed consent from the patient for publishing her medical details was obtained.

ORCID

Lili Zhi  <https://orcid.org/0000-0001-5664-9974>

REFERENCES

1. Harb H, Chatila TA. Mechanisms of Dupilumab. *Clin Exp Allergy*. 2020;50(1):5-14.

2. Castro M, Corren J, Pavord ID, et al. Dupilumab efficacy and safety in moderate-to-severe uncontrolled asthma. *N Engl J Med*. 2018;378(26):2486-2496.
3. Pourang A, Mesinkovska NA. New and emerging therapies for alopecia areata. *Drugs*. 2020;80(7):635-646.
4. Guttman-Yassky E, Renert-Yuval Y, Bares J, et al. Phase 2a randomized clinical trial of dupilumab (anti-IL-4R α) for alopecia areata patients. *Allergy*. 2022;77(3):897-906.
5. Simakou T, Butcher JP, Reid S, Henriquez FL. Alopecia areata: a multifactorial autoimmune condition. *J Autoimmun*. 2019;98:74-85.
6. Zhou C, Li X, Wang C, Zhang J. Alopecia areata: an update on etio-pathogenesis, diagnosis, and management. *Clin Rev Allergy Immunol*. 2021;61(3):403-423.
7. Rajabi F, Drake LA, Senna MM, Rezaei N. Alopecia areata: a review of disease pathogenesis. *Br J Dermatol*. 2018;179(5):1033-1048.
8. Fukuyama M, Ito T, Ohyama M. Alopecia areata: current understanding of the pathophysiology and update on therapeutic approaches, featuring the Japanese dermatological association guidelines. *J Dermatol*. 2022;49(1):19-36.
9. Magen E. Alopecia areata after omalizumab treatment for chronic spontaneous urticaria. *Acta Derm Venereol*. 2019;99(10):919-920.
10. Jin P, Gao M, Miao X, Wang Q, Zhi L. Transient alopecia areata following treatment with omalizumab in a patient with asthma and nasal polyps: a potential dermatological adverse event. *J Cosmet Dermatol*. 2021. online ahead of print.

How to cite this article: Jin P, Wei L, Zhang Q, et al.. Dupilumab for alopecia areata treatment: A double-edged sword?. *J Cosmet Dermatol*. 2022;00:1-3. doi: [10.1111/jocd.15136](https://doi.org/10.1111/jocd.15136)