SKIN

BRIEF ARTICLE

Significant Improvement of Persistent Hailey-Hailey Disease with Dupilumab: A Case Report

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ABSTRACT

Hailey-Hailey disease is a rare, genetic blistering disease characterized by erythematous, scaly plaques in intertriginous regions such as the axillary, inframammary, and groin regions. The plaques cause discomfort and are difficult to treat. Treatment ranges from topical to systemic and includes topical steroids such as triamcinolone and hydrocortisone, topical tacrolimus, zinc paste, lidocaine cream, oral antibiotics such as doxycycline and minocycline, and oral naltrexone being commonly used options. Despite the variety of treatment options, Hailey-Hailey disease is notoriously difficult to treat with each patient responding uniquely to treatment. There has been evidence of patients with Hailey-Hailey disease experiencing improvement of symptoms with dupilumab injections. Dupilumab has several off-label uses, including allergic contact dermatitis, hand dermatitis, chronic spontaneous urticaria, and alopecia areata, showing promise for its use in dermatology outside of atopic dermatitis and prurigo nodularis. Due to its minimal side effects, dupilumab can be tried for Hailey-Hailey disease with little risk. We present the case of a 37-year-old female with recalcitrant Hailey-Hailey disease who noticed significant improvement on dupilumab.

INTRODUCTION

Hailey-Hailey disease (HHD) is an autosomal dominant genetic blistering disease and is caused by defective intracellular calcium homeostasis.[1] The disease manifests as erythematous, scaly plaques and is often triggered by moisture and friction in intertriginous regions (axillary, inframammary, and groin regions).[1] These lesions cause severe discomfort and commonly flare in the hot summer months. Treatment options include topical steroids, tacrolimus, zinc paste, lidocaine cream, oral antibiotics, and oral naltrexone. Additionally, each patient may have a different response to the treatment modality leaving no consistent treatment plan. Therefore, dermatologists should choose the appropriate option for each patient's unique case.[2]

There has been some evidence of patients with recalcitrant HHD experiencing improvement of symptoms with dupilumab injections.[3,4] Dupilumab has several off label uses, including allergic contact dermatitis, hand dermatitis, chronic spontaneous urticaria, and alopecia areata, showing promise for its use in dermatology outside of atopic dermatitis and prurigo nodularis.[5] Due

to its minimal side effects, dupilumab can be tried for HHD with little risk. We examine this further in our patient with recalcitrant HHD.

CASE REPORT

We present a 37-year-old female with a long personal and family history of HHD, mainly involving the axillary folds and inframammary region. The patient did not require a biopsy for diagnosis as her father and sister had biopsy confirmed HHD. She had failed several treatments including topical triamcinolone, topical aluminum chloride, topical tacrolimus, oral naltrexone, and oral doxycycline and struggled with HHD for years with little relief. She noticed slight improvement with low dose oral naltrexone but found the gastrointestinal side effects difficult to tolerate and noticed no improvement at all with the topical triamcinolone or topical tacrolimus. Noted severe burning and exacerbation of symptoms with topical aluminum chloride and found oral doxycycline difficult to tolerate due to diarrhea. She reported decreased sweat and improvement of symptoms in cooler winter months. She used mepilex dressings daily, as well as ice packs and Vicks rub for symptomatic relief of the burning.

On exam, active erythematous and scaly plaques were noted in the bilateral axilla, while plaques under her right breast were well controlled. She had dealt with the symptoms for years with expansion of the rash.

We then started our patient on dupilumab 300 mg subcutaneous injection every two weeks with an initial 600 mg loading dose. She returned for follow-up 4 months later and noted significant improvement of her axillary regions (**Figure 1 and 2**) but noted flaring in her right inframammary region (**Figure 3**). She also received 0.5 ml of intralesional 3 mg/mL triamcinolone to the flared area during the follow-up visit. She found dupilumab easy to tolerate and opted to continue treatment. We plan to continue dupilumab and follow-up in 3 months.

DISCUSSION

Our patient's distribution of lesions and family history are consistent with HHD. She noticed significant improvement of both axillae after 4 months of dupilumab but noticed flaring of her inframammary region which was previously well controlled. There is evidence of patients with HHD noticing improvement of symptoms with dupilumab injections.[3,4]

One case series noted improvement in patients with HHD in an average of 2 months of dupilumab with sustained improvement years later.[3] HHD has historically been rare and difficult to treat, with patients often failing several treatment options.[2] Commonly used treatments include topical steroids, topical tacrolimus, zinc paste, lidocaine cream, oral antibiotics, and oral naltrexone. Surgical options with lasers and ablative therapy are present as well for recalcitrant cases.[6] There is no commonly used treatment regimen for HHD and since each patient may respond uniquely to different treatments there is no standard of care for patients with HHD.[2] Additionally, there is not extensive evidence in the literature to support a particular treatment option due to the rarity of the condition. Further, minimizing the triggers of friction and sweat are important with our patient noticing improvement in cooler, winter conditions.

Dupilumab works to block IL-4*a* and IL-13 production and is used to treat asthma and atopic dermatitis, amongst other conditions.[5] The IL-4 and IL-13 pathways

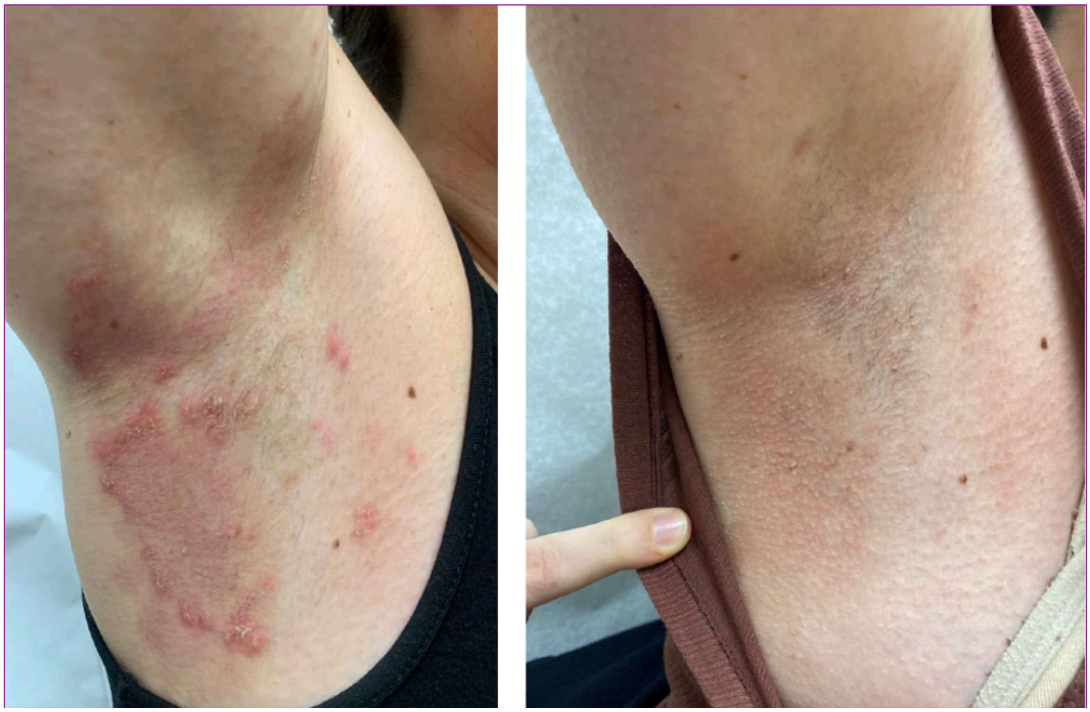

Figure 1. Left: Widespread erythema and scaly plaques seen in right axilla. Right: Notable improvement in size and erythema of lesions after 4 months of dupilumab.

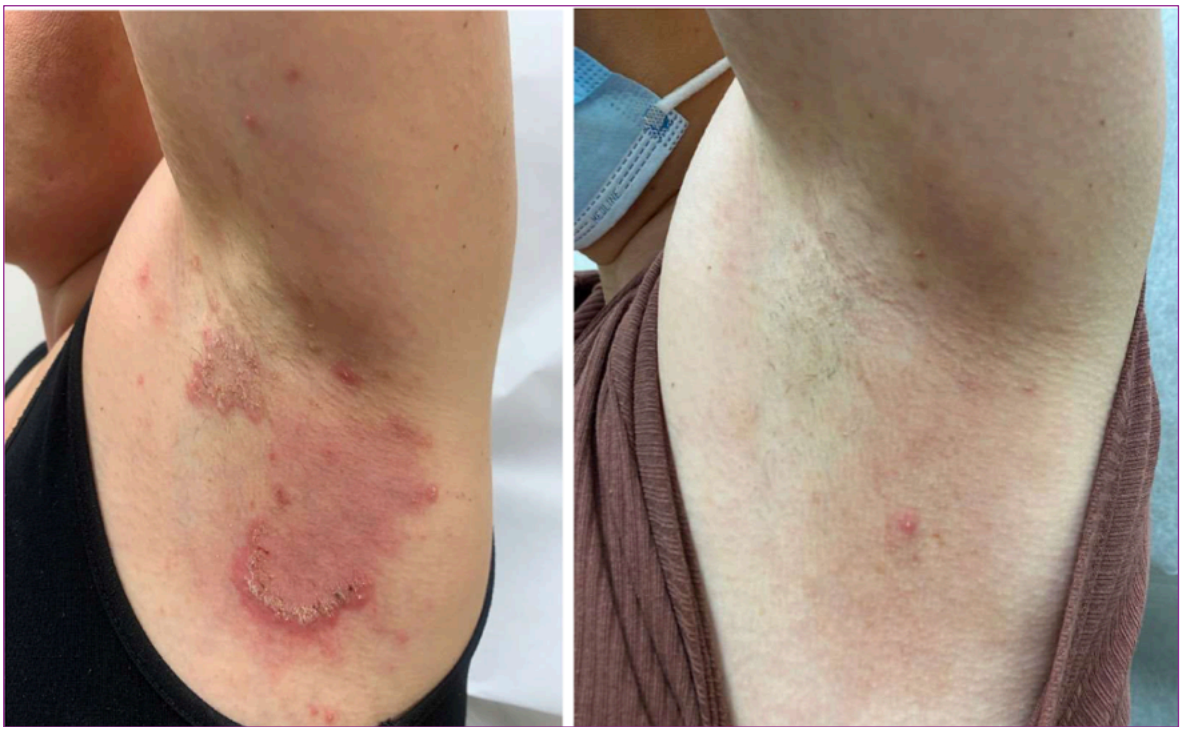

Figure 2. **Left**: Erythema and scaly plaques with mild crusting seen in left axillary region. **Right**: Significant improvement seen after 4 months of dupilumab.

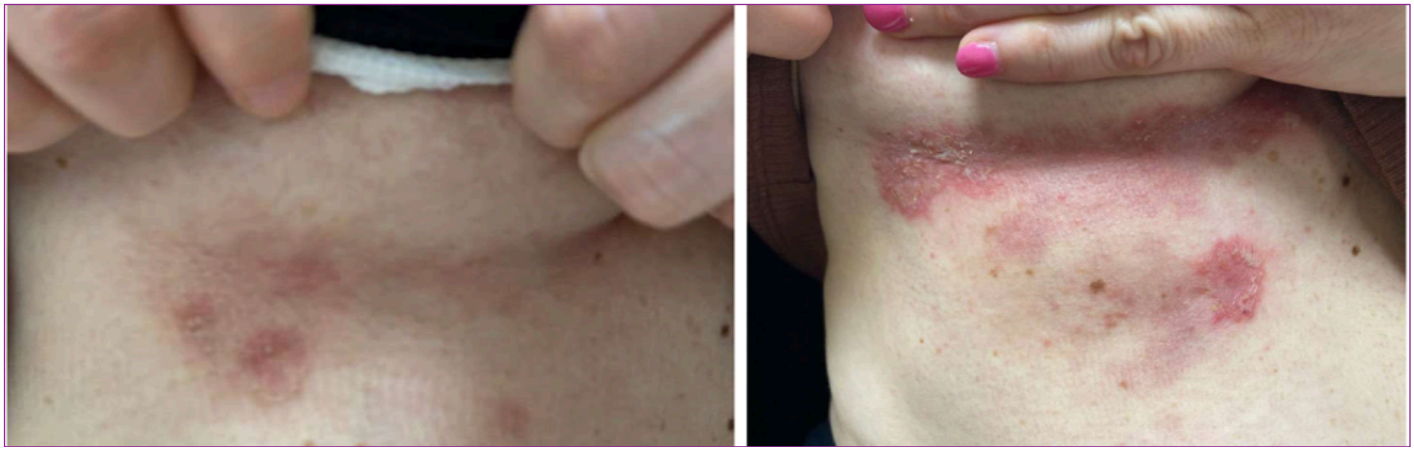

Figure 3. Left Small erythematous lesions seen in right inframammary area. Right: Erythematous scaly plaques seen in right inframammary after 4 months of dupilumab.

stimulate eotaxin-3 which inhibits the release of free intracellular calcium and subsequent actin polymerization.[1] Since HHD is also characterized by inhibited calcium release and actin polymerization, it seems blockage of IL-4 and IL-13 via dupilumab could restore calcium signaling in the cell.[4,6] Further research may be able to determine the overall effectiveness and mechanism of action of dupilumab injections in patients with HHD.

While our patient noted significant improvement of stubborn areas, she also flared in others that were previously well controlled. Increasing dose frequency may be beneficial and further studies may determine the optimal dosage and frequency of dupilumab injections for HHD. Dupilumab is worth investigating further as a treatment option for patients with HHD who have failed traditional therapies and may become a potential mainstay of treatment.

Conflict of Interest Disclosures: None

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References:

1. Hu Z, Bonifas J, Beech J *et al*. Mutations in *ATP2C1*, encoding a calcium pump, cause Hailey-Hailey disease. *Nat Genet* 2000; 24:61–5.
2. Hailey-Hailey Disease: What treatment should we choose? Crossref DOI link: https://doi.org/10.1016/j.jaad.2018.05.616
3. F. Alamon-Reig, L. Serra-García, X. Bosch-Amate, C. Riquelme-Mc Loughlin, J.M. Mascaró, Dupilumab in Hailey-Hailey disease: a case series, Journal of the European Academy of Dermatology and Venereology, 10.1111/jdv.18350, 36, 10, (e776-e779), (2022).
4. Alzahrani N, Grossman-Kranseler J, Swali R, Fiumara K, Zancanaro P, Tyring S, Rosmarin D. Hailey-Hailey disease treated with dupilumab: a case series. Br J Dermatol.
5. Maloney NJ, Tegtmeyer K, Zhao J, Worswick S. Dupilumab in Dermatology: Potential for Uses Beyond Atopic Dermatitis. J Drugs Dermatol. 2019 Oct 1;18(10):S1545961619P1053X. PMID: 31603635.
6. Jia F, Zhao Q, Shi P, Liu H, Zhang F. Dupilumab: Advances in the off-label usage of IL4/IL13

antagonist in dermatoses. Dermatol Ther. 2022 Dec;35(12):e15924. doi: 10.1111/dth.15924. Epub 2022 Oct 20. PMID: 36219538.