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Case Report

Dupilumab as a treatment for a case of benign familial pemphigus

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ABSTRACT

Hailey-Hailey disease (HHD) is an uncommon autosomal dominant genodermatosis characterized by recurrent blistering eruptions primarily affecting intertriginous areas, leading to the formation of eroded, erythematous plaques within flexural skin folds. The condition significantly impairs quality of life due to the frequency of infections, exacerbated by the limited and often ineffective therapeutic options currently available for HHD. In this report, we present a compelling case of HHD successfully treated with dupilumab, highlighting remarkable improvement observed within just two weeks of initiating treatment with this novel therapeutic agent. This promising outcome underscores the potential of dupilumab in managing challenging cases of HHD and warrants further exploration in larger clinical trials.

Keywords: HHD, Dupilumab, Genodermatosis

INTRODUCTION

Hailey-Hailey disease (HHD) is a rare autosomal dominant genodermatosis characterized by recurrent blistering eruptions in intertriginous areas that form eroded, erythematous plaques and painful rhagades in flexural skin.[1,2] HHD is caused by mutations in the ATP2C1 gene on chromosome 3 that encodes a calcium pump of the Golgi apparatus, which is essential for desmosome function in keratinocytes.[1,2] Inadequate function of the 2B isoform of the endoplasmic reticulum Ca^{2+}ATPase leads to aberrant Ca^{2+} signaling.[1] As a result, lack of calcium deposition in the Golgi leads to dysfunction and disrupts protein processing, resulting in desmosomal separation and weakened keratinocyte adhesion, ultimately causing intraepidermal acantholysis and dyskeratosis in the stratum spinosum.[1,2]

HHD is a chronic debilitating disease with no curative treatment with a significant impact on a patient's quality of life due to the few therapeutic options with limited efficacy. First-line therapies include topical and systemic steroids as well as topical and systemic antibiotics and antifungals.[1,2] Second-line therapies include topical calcineurin inhibitors, oral retinoids, CO_2, and immunosuppressive agents.[1,2] Cases of HHD treated with biological therapies and small molecules have been described, but are few and vary considerably with efficacy and onset of action.[3-5]

CASE REPORT

This case report presents the successful treatment of Hailey-Hailey with dupilumab. This is a 63-year-old man with a 20+ year biopsy proven history and family history of HHD that presented to the clinic with painful, chronic erosive erythematous plaques and maceration in the axillae and inguinal canal. He had been previously treated in the past with topical corticosteroids, systemic steroids, and oral antifungal therapy with oral antifungal therapy being the most effective. The patient was initially treated medium to high potency topical steroids and oral

fluconazole without adequate response. A month later, he was started on oral fluconazole, topical ketoconazole 2% cream, tacrolimus ointment, and intramuscular triamcinolone 40 mg, which had little to no impact on his disease state. Two weeks later, a trial of CO_2 laser ablation and oral cephalexin was initiated without improvement. Dupilumab was initiated four months after he was initially seen in our clinic. Two weeks after initiating dupilumab, the patient had a significant reduction of the erythematous plaques, erosions and maceration in the axillae (Figure 1). The patient was seen 1 month later and had almost complete resolution of pain and erythematous plaques on the axillae and inguinal folds without any side effects (Figure 1).

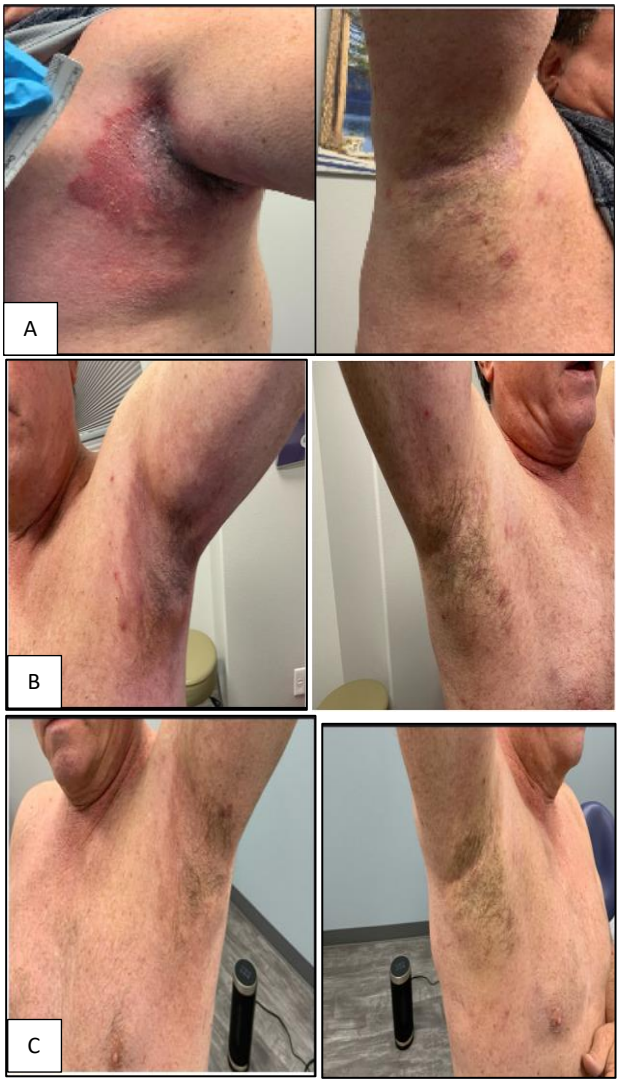

Figure 1 (A-C): HHD at baseline left and right axilla; 2 weeks after initiating dupilumab and 1 month after dupilumab.

DISCUSSION

Dupilumab, a humanized IgG4 monoclonal antibody, disrupts the IL-4 signaling pathway specifically targeting the shared IL-4 receptor alpha chain (IL-4Ra) on both type 1 and type 2 IL-4 receptor complexes[6]. While the precise mechanism of HHD remains unknown, it is possible that the disrupted skin barrier and acantholysis in HHD create a microenvironment conducive for Th2 inflammation, where IL-4 as seen in other inflammatory conditions, plays a role. Previous case series postulate that dupilumab's efficacy is linked to its influence on modulating intracellular calcium through an interaction between C-C motif chemokine ligand 26 (CCL26) and its receptor, C-C chemokine receptor type 3 (CCR3); the role of CCL26 and CCR3 in activating eosinophils, basophils and Th2 cells might be countered by a novel function of suppressing intracellular calcium release.[7]

In the literature there are cases of HHD treated with dupilumab alone[5], but none to our knowledge with a rapid response time of 2 weeks and sustained results at 1 month. While early results with dupilumab for HHD are encouraging, larger clinical trials are needed to definitively establish its efficacy and safety profile before it can be considered a standard treatment option.

CONCLUSION

Dupilumab represents a promising therapeutic option for HHD, demonstrating significant efficacy in managing symptoms and improving patients' quality of life. By targeting the underlying mechanisms of inflammation and keratinocyte dysfunction, dupilumab offers a novel approach to treating this challenging dermatological condition. Continued research and clinical trials are essential to further establish its long-term safety and efficacy profiles, but current evidence suggests that dupilumab holds considerable potential as a valuable addition to the treatment armamentarium for HHD.

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