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CASE AND RESEARCH LETTER

Successful Treatment of Hailey-Hailey Disease With Dupilumab

Tratamiento exitoso de la efermedad de Hailey-Hailey con dupilumab

To the Editor:

Hailey-Hailey disease is a genodermatosis of autosomal dominant transmission, caused by loss-of-function mutations in the ATP2C1 gene. Failure of a proper intracellular calcium homeostasis, particularly in the Golgi apparatus, is responsible for a weakened desmosomal adhesion between keratinocytes. Thus, acantholysis of stratum spinosum occurs, causing a chronic clinical appearance of flaccid blisters and malodourous erosions in intertriginous areas. Chronic pruritus is also frequently present and difficult to treat, contributing to the severe burden of the disease.

A 57-year-old woman suffered from Hailey-Hailey disease since early adulthood, which was refractory to several different topical and systemic treatments, including a recently described novel approach with low-dose naltrexone.[1] She had malodourous bilateral hyperkeratotic papules and erosions on axillae, inframammary and abdominal folds (Fig. 1a). Pruritus was her main complaint, as it was persistent, intense (Numeric Rating Scale itch 8/10) and disruptive of both her sleep quality and social life.

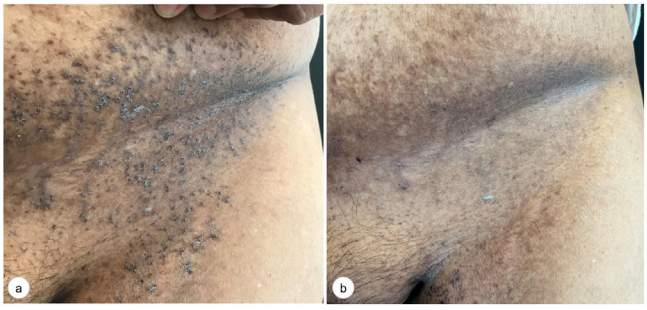

Figure 1 Clinical pictures of Hailey-Hailey disease lesions on inferior abdominal skin fold at week 0 (a) and week 12 (b).

Dupilumab 300 mg every other week was started after a 600 mg loading dose. Both pruritus and sleep quality drastically improved after only one week of treatment. Additionally, significant healing of the skin lesions was noticeable by week 12, with reduction in size and thickness of previous hyperkeratotic papules and erosions (Fig. 1b). Treatment was well tolerated, and the patient is satisfied with the outcome.

Our case reflects a remarkable improvement with dupilumab, a fully human monoclonal antibody against interleukins (IL) 4 and 13, on both subjective and objective findings in Hailey-Hailey disease, thus corroborating the findings by Alzahrani et al.[2] This drug is currently approved for moderate-to-severe atopic dermatitis, showing significant reduction of pruritus right after the induction phase. Even though the mechanism of dupilumab on Hailey-Hailey disease is still unknown, it is possible that the inhibition of IL-4 and IL-13 modulates favourably the intracellular calcium signalling,[2] thus compensating its genetic defect. Furthermore, we emphasize the central role of IL-4 as a neuromodulator on chronic pruritus, which is responsible for amplifying responses to minor pruritogenic agents.[3,4] The expression of IL-4 receptors on sensory neurons of the dorsal root ganglion[4] further corroborates the relevance of this molecule in chronic pruritus.

In summary, we highlight dupilumab's innovative role on managing symptoms and objective findings in patients with Hailey-Hailey disease. It is possible that this positive effect could be extrapolated to other dyskeratosis with severe pruritus, but further investigation is needed.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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