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Hailey-Hailey Disease: A Case Report

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Received: 23 November 2024 | **Revised:** 6 March 2025 | **Accepted:** 5 April 2025

Funding: The authors received no specific funding for this work.

Keywords: corticosteroids | flexural areas | Hailey-Hailey disease | histopathology | vesicular lesions

ABSTRACT

Hailey-Hailey disease should be considered in patients with recurrent, painful, pruritic, vesicular lesions in flexural areas. Early diagnosis through histopathology and immunofluorescence allows effective management with corticosteroids, emollients, and lifestyle modifications, leading to significant improvement and symptom resolution.

1 | Introduction

Hailey–Hailey disease (HHD), also known as familial benign chronic pemphigus, was first described in 1939 by Howard and Hugh Hailey [1]. It is a rare blistering autosomal dominant dermatological disease that affects around 1/50,000 of the general population and occurs equally in both males and females. The disease often has a remitting–relapsing pattern and becomes more noticeable during the third/fourth decade of life, although it can occur at any age [2]. The symptoms are usually characterized by scaly erosive crusts, malodorous, painful blistering rashes with thickened macerated fissures, recurrent bullous and flaccid ruptured vesicles resulting in erythematous plaques with varying degrees of redness and are generally prompted by excessive sweating, local infections, and/or friction with a predilection for flexural areas localized especially to the neck, axillary, and inguinal regions, which often become infected, significantly impairing patients quality of life [3]. We report a case of Hailey–Hailey disease (HHD) in a 40-yearyear-old female with complete coverage of clinical features, investigation, treatment, and follow-up.

2 | Case Presentation

2.1 | Case History/Examination

A 40-year-old woman presented to the clinic with a 20-day history of foul-smelling, itchy lesions located in the flexural folds, including the neck folds, inframammary folds, axillary folds, and antecubital fossa bilaterally. The patient described the lesions as starting with the development of fluid-filled vesicles, about 8–10 in number, each approximately 0.5 cm in size. These vesicles began in the neck region and progressively increased in size, forming flaccid bullae. Over time, the lesions spread towards the chest, involving the inframammary fold, axillary fold, truncal surface, and gluteal region. The vesicles were painful, pruritic, and associated with a stinging and burning sensation, which significantly contributed to the patient's discomfort. Additionally, the lesions discharged a malodorous fluid, which further aggravated the symptoms.

The patient reported that each vesicle lasted for 1 day, after which it spontaneously ruptured, leaving behind erythematous,

eroded, and macerated plaques. Over time, the skin became increasingly damaged due to scratching. She mentioned that she had similar lesions below both breasts and in the axillary regions for the past 2 years, which were treated with multiple courses of antimicrobials, corticosteroids, and antifungals, yielding only partial relief.

She also gave a history of photosensitivity, but she was not taking any other medications aside from antihypertensive treatment for managing hypertension for the past 2 years. On examination, the patient had no significant findings related to her nails, mucosa, scalp, palms, or soles. Dermatological examination revealed multiple crusted erythematous excoriated erosions and macerated plaques distributed symmetrically over the intertriginous areas, such as the neck folds, axillary folds, antecubital fossa, inframammary folds, and gluteal folds (Figure 1). Notably, there was post-inflammatory hyperpigmentation observed below the right breast, which was symmetrical with the active lesion on the left side. Nikolsky's sign was negative. A solitary erosion was noted on the right forearm, surrounded by erythema. There were no mucosal, nail, scalp, or systemic signs that pointed toward any other bullous disorders or systemic conditions.

3 | Methods (Differential Diagnosis, Investigations and Treatment)

Given the clinical presentation, Hailey-Hailey disease was strongly suspected. To confirm the diagnosis, a skin biopsy was performed from an active inframammary lesion. Histopathological examination revealed the epidermis with mild orthokeratosis and intraepithelial neutrophils. The hallmark feature was the presence of suprabasal clefts, accompanied by acantholytic cells, which appeared with a dilapidated brick-wall appearance, characteristic of Hailey-Hailey disease (Figure 2). In addition, the superficial dermis showed mild neutrophilic and lymphocytic infiltration, while the deeper dermis and subcutis were unremarkable. The findings were highly suggestive of Hailey-Hailey disease, which is an autosomal dominant disorder that causes intraepidermal blistering and acantholysis.

To further investigate the etiology, a direct immunofluorescence test was performed on a non-lesional specimen, which showed no immune reactants. However, linear C3 deposits were found along the basement membrane, which is typical for this condition.

Routine laboratory investigations, including hemogram, liver function tests, renal function tests, and serum lipid profile, all returned normal results. A Tzanck smear of the lesions demonstrated a few acantholytic cells, which further supported the clinical suspicion of Hailey-Hailey disease. There were no abnormal findings in the systemic examination. Given the clinical and histopathological evidence, differential diagnoses such as pemphigus vulgaris, fungal infections, bacterial infections (including impetigo), and contact dermatitis were considered, but Hailey-Hailey disease was deemed the most likely diagnosis.

After confirming the diagnosis of Hailey-Hailey disease through clinical examination and histopathology, a treatment plan was initiated. The patient was started on a moderate-potency oral corticosteroid regimen (Wysolone 60 mg once daily for 2 weeks), which was then tapered to 10 mg daily over the next 15 days. This treatment aimed to reduce inflammation and control the acute flare-ups of the disease. In addition to the oral corticosteroids, the patient was prescribed Clonate-F cream, a topical corticosteroid, to apply locally to the affected areas. Emollients were also recommended to keep the skin moisturized and to improve skin hydration, which would help to reduce irritation and prevent further exacerbations.

To address the potential secondary bacterial infection and inflammation, the patient was given oral antibiotics, Amoxiclav 625 mg twice daily for 5 days. Along with pharmacologic treatment, the patient was counseled on measures to reduce skin friction and moisture in the flexural areas. Advice included

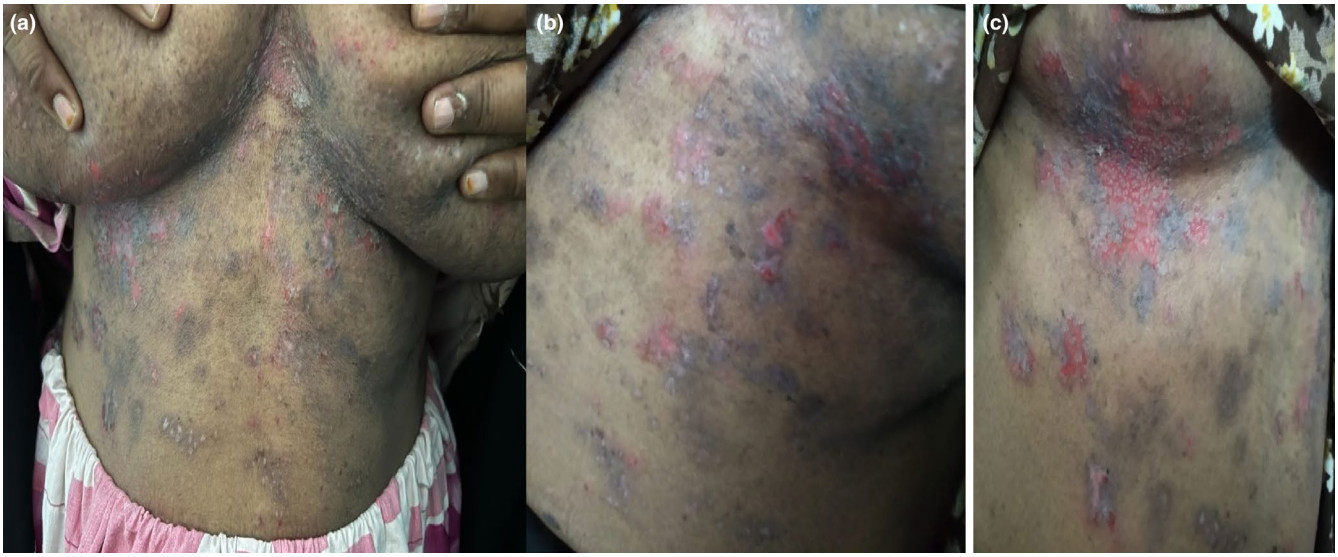

FIGURE 1 | Skin lesions at the time of exacerbation: Vesicles, pustules, and crusted plaques on (a) inframammary region, (b) left upper thigh, and (c) gluteal region.

wearing loose, cool clothing, using absorbent pads in skin folds, and keeping the affected areas dry to prevent further irritation. This combination therapy allowed for better symptom control in the short term, which led to a significant improvement in the patient's condition.

4 | Results (Outcome and Follow-Up)

Within 4 weeks of starting the treatment regimen, the patient showed significant improvement in her skin lesions. The vesicles and bullae gradually resolved, and the erythematous, macerated plaques began to heal. By the time of the six-month follow-up, there was complete regression of the skin lesions, with no new lesions appearing. The patient reported feeling much more comfortable, with no further discomfort from stinging, burning, or pruritus.

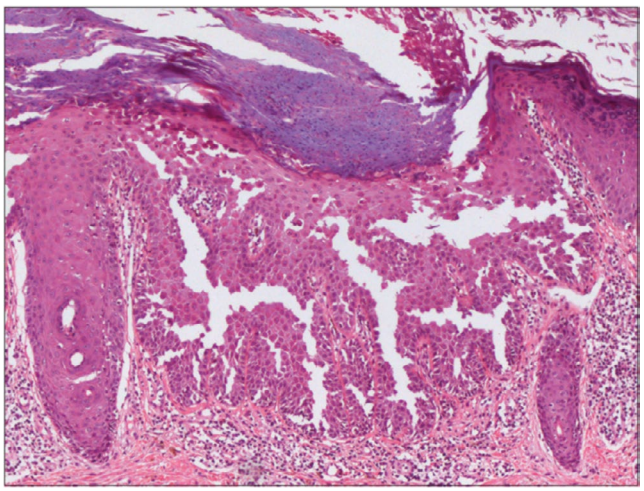

FIGURE 2 | Histopathology showing dilapidated brick wall appearance with suprabasal clefts and acantholytic cells (H and E, 10×).

Emollients and oral multivitamins were continued twice daily for a total of 3 months to maintain skin hydration and support overall skin health. During follow-up visits, the patient did not experience any relapse or recurrence of lesions, and she tolerated the medications well, without any significant side effects. She was advised to continue with the use of emollients and protective measures in the future to minimize the risk of flare-ups. At the end of the six-month follow-up period, the patient had no further signs or symptoms of Hailey-Hailey disease, indicating a favorable long-term outcome (Figure 3).

5 | Discussion

Hailey-Hailey disease is a bullous disorder characterized by the development of blisters, warty papules, and flexural erosions. The pathogenesis is linked to a mutation of the ATP2C1 gene that codes for chromosome 3q21, which encodes an ATP powered intracellular calcium ion transporter protein pump on the golgi complex of epidermal cells, leading to disrupted calcium signaling, altering epidermal integrity between the keratinocytes and desmosomes, causing an imbalance in the homeostasis of the ion, resulting in intraepidermal acantholysis [4, 5]. Clinically, it can be misdiagnosed as inverse psoriasis, tinea, impetigo, contact dermatitis, eczema, intertrigo, erythrasma, pemphigus vulgaris, linear Ig A disease, dermatophytosis, and atypical Darier's disease [6]. Occasionally, the erosions spread centrifugally with an active inflammatory border in serpiginous patterns, as seen in our case. The lesions generally regress in a few weeks and some lesions follow a chronic course. Less commonly involved sites are the scalp, antecubital or popliteal fossa. Our patient had a solitary bulla creating an erosion over the right forearm and on the upper thigh are the uncommon sites of involvement. Histologically partial loss of the intercellular bridges between keratinocytes gives a dilapidated brick wall appearance to the epidermis with fewer dyskeratotic cells. A red dyskeratotic rim around the nucleus is distinctive and

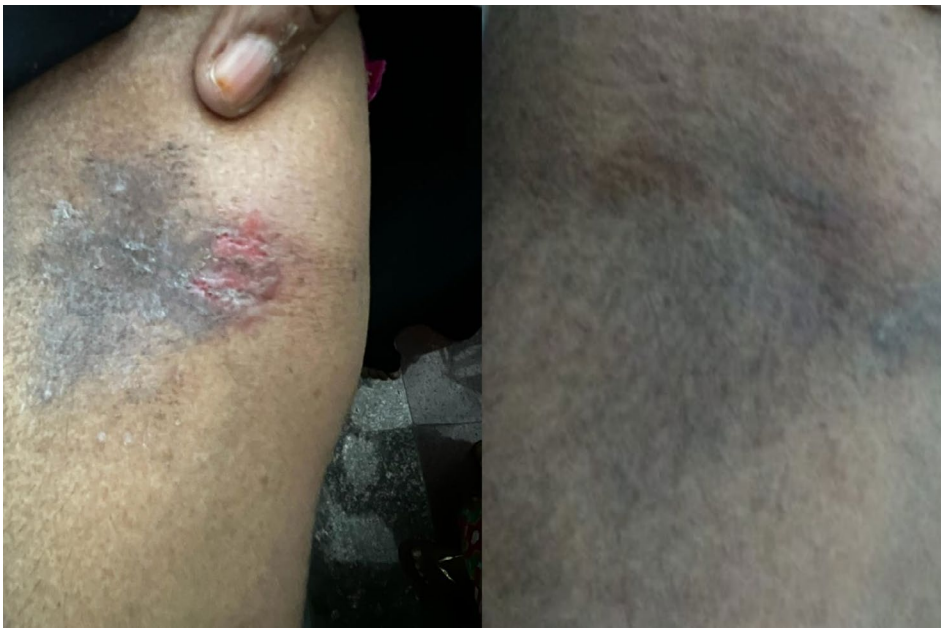

FIGURE 3 | Solitary skin lesion on right arm before treatment and regression of lesion after treatment is shown.

helps to distinguish HHD from other acantholytic disorders [7]. Direct immunofluorescence is negative. Rare case reports have described C3C deposits at dermal-epidermal junctions [8]. Superinfection with bacteria like staphylococcus species, fungi like candidiasis, and viruses play a significant role in exacerbations and persistence of lesions. The disease is associated with serious psychological distress and can severely affect the quality of social life of patients [9]. Despite progress in our understanding of the molecular genetics of HHD, unfortunately, the response has been variable and existing treatments do not provide a long lasting positive therapeutic benefit [10]. There are various treatment modalities for HHD, including topical corticosteroids, oral and topical antimicrobials and/or topical antimycotics therapy, retinoids, glycopyrrolate, naltrexone, botulinum toxin Type A and modern treatment options include use of topical immunomodulators like Calcineurin inhibitors (cyclosporin A, tacrolimus and pimecrolimus) and interventional methods like laser ablation, dermabrasion, photodynamic therapy, electron beam radiotherapy and application of Narrow-band (NB) ultraviolet B (UVB) [11–13]. Care should be taken with chronic use of corticosteroids as it may lead to skin atrophy, striae distensae and telangiectasia. Additionally, patients with Hailey-Hailey are instructed to avoid conditions such as friction, sunburn and sweating, and to keep the affected areas dry. Cool compresses and dressing have shown they can be effective in treating swelling, redness, and intensity of the blisters [2]. HHD cases involving large skin areas have been rarely reported as generalized HHD [14]. Hence here's a case of generalized HHD successfully treated with oral antimicrobials, oral steroids, topical steroids, emollients, and multivitamins.

6 | Conclusion

Clinicians generally have limited experience with HHD patients, and the lack of a strong evidence base can make counseling and treatment of affected individuals difficult. Furthermore, the chronic and recalcitrant nature of HHD greatly impacts a patient's quality of life, making its management challenging for dermatologists. In conclusion, physicians should keep in mind HHD during daily practice as a differential diagnosis.

Author Contributions

Romana Riyaz: conceptualization, writing – original draft, writing – review and editing. **Sajjad Ahmed Khan:** conceptualization, writing – original draft, writing – review and editing. **Sarfaraj Ahamad Khan:** writing – original draft. **Jyoti Shah:** writing – original draft. **Durgeshlal Chaudhary:** writing – original draft.

Acknowledgments

Authors are thankful to the department of radiology as well as the department of cardiovascular medicine for providing the needful information. We express our gratitude to the patient's family members for their cooperation.

Consent

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data will be provided by the corresponding author upon reasonable request. Images are uploaded in the separate files.

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