

# CASE REPORT

## HAILEY- HAILEY DISEASE: 2 CASE REPORTS

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**ABSTRACT:** Hailey-Hailey disease is an autosomal dominant acantholytic disorder relatively uncommon in India. It is characterized by painful, pruritic, foul smelling vesicles and bullous lesions with erosions in intertriginous areas such as the neck, axillae, inframammary areas and groin. The defect in ATPC2 gene leads to calcium channel dysfunction which results in defect in epidermis. Fungal infection, intertrigo, psoriasis, extramammary Paget's disease, acanthosis nigricans, pemphigus vegetans and Darier's disease are some of the dermatosis from which it needs to be differentiated. Histopathology has a key role in diagnosis of Hailey-Hailey disease with characteristic 'dilapidated brick wall' appearance. Hailey-Hailey disease can be easily misdiagnosed by general physicians due to lack of knowledge of this uncommon disease as it resembles dermatosis involving intertriginous areas. Due to its relapsing and remitting course there is a need to have effective treatment options. Two cases of Hailey-Hailey disease are presented here.

**KEYWORDS:** Hailey-Hailey disease, Dilapidated brick wall, Intertriginous areas.

**KEYMESSAGES:** Physicians must keep this disease as a differential diagnosis in resistant intertriginous dermatosis especially when there is a positive family history.

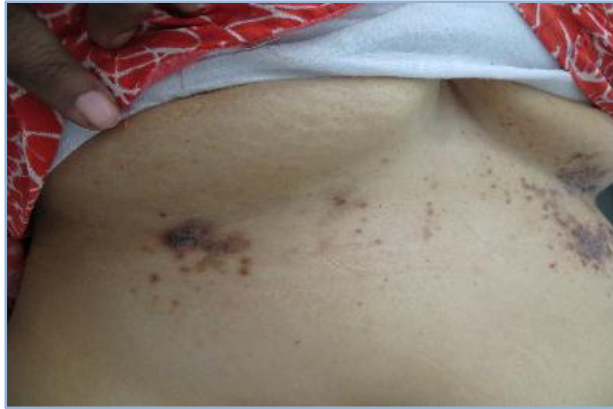
**INTRODUCTION:** Hailey-Hailey disease (HHD) is a rare autosomal dominant acantholytic disorder which recurs with remitting and relapsing episodes.<sup>[1]</sup> The defect in ATPC2 gene leads to calcium channel dysfunction which results in defect in epidermis. It is characterized by painful, pruritic, foul smelling vesicles and bullous lesions with erosions in intertriginous areas. Lesions get aggravated by friction, ultraviolet radiation, warmth, moisture and superficial bacterial, viral or fungal infections.<sup>[2]</sup> Histopathology has a key role in diagnosis of Hailey-Hailey disease. Topical modalities of treatment are antibiotics, steroids, tacalcitol another vitamin D3 derivative and tacrolimus while systemic treatment includes antibiotics, steroids, cyclosporine, dapsone, methotrexate and thalidomide. Two cases of Hailey-Hailey disease is presented here with characteristic histopathological features to highlight the importance of early diagnosis.

**CASE HISTORY: Case 1:** A 41 year's old married Indian female presented with lesions under breasts and in groins since 3 years associated with itching. H/o fluid filled lesions prior to presenting lesions were present. Many types of treatment in the form of topical and systemic drugs were taken with no improvement. Similar type of complaints in father was present. H/o summer aggravation was present. On examination multiple discrete hyperpigmented papules over bilateral inframammary regions and groins [Figure-1a & b]. No mucosal involvement or nail changes present.

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**Fig.1a:** Multiple discrete hyperpigmented papules over bilateral inframammary region.



**Figure 1a**

**Fig.1b:** Multiple discrete hyperpigmented papules over bilateral groins.



**Figure 1b**

Biopsy taken from the lesion over groin showed thinned out epidermis with presence of suprabasal vesicles containing keratinocyte and inflammatory infiltrate of neutrophils and lymphocytes. The villi (Elongated papilli) are lined by single layer basal cells, protruding up grade into vesicles. A narrow layer of epidermal cells proliferating downward into dermis is seen. Upper dermis shows mononuclear cell inflammatory infiltrate. Changes were suggestive of Hailey-Hailey disease. Immunofluorescence test, due to unavailability, was not done in our set up. Patient was treated with oral doxycycline and topical clobetasol propionate 0.05% cream for 15 days. Lesions resolved, patient was then given betamethasone valerate and tacrolimus 0.1% ointment to be continued.

**Case 2:** A female, 65 years presented with multiple eruptions over flexural areas of the body, since almost 35 to 40 years with itching and burning sensation. H/o recurrent relapses in summer, with winter remissions was present. No specific family history was noted. O/E multiple papular lesions forming plaques with maceration and malodorous odour in axilla, groins, submammary regions, neck and flexors of elbow and knee joints [Figure-2 a & b].

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**Fig. 2a:** Multiple papular lesions forming plaques with maceration in groins.



**Figure 2a**

**Fig. 2b:** Multiple papular lesions forming plaques with maceration in axilla.



**Figure 2b**

At few places lesions were verrucous. Patient was obese with no other co-morbid condition. No orogenital involvement or nail changes. Histopathological examination showed suprabasal separation producing lacunae (Bullae). Villi characterized by elongated papillae lined by single layer of basal cells seen protruding upward in the bulla. Many cells of the detached stratum malphighii shows loss of intercellular bridges leading to acantholysis. Despite acantholysis the cells in the lacunae have few intact intercellular bridges giving a dilapidated brick wall appearance. The acantholytic cells have homogenised cytoplasm, hyperkeratosis and hypogranulosis. Dermis shows mild chronic inflammation.

(Fig-3a-10X, 3b-40x) Changes were suggestive of Hailey-Hailey disease. Patient was given oral dapsone (100mg) daily, oral antibiotics, antifungal to prevent secondary fungal infection and topical steroids. After a month of follow up when lesions resolved, topical steroid was replaced by tacrolimus (0.03%).

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**Fig.3a:** Suprabasal separation producing lacunae (bullae). Loss of intercellular bridges leading to acantholysis with few intact intercellular bridges giving a delapidated brick wall appearance. 10X (H & E stain)

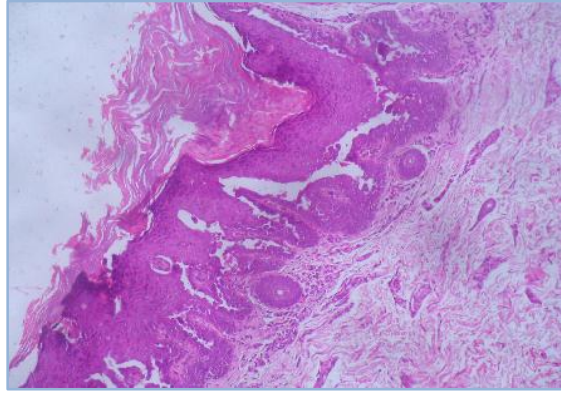


Figure 3a

**Fig. 3b:** Loss of intercellular bridges leading to acantholysis with few intact intercellular bridges giving a delapidated brick wall appearance. 40X (H& E stain)

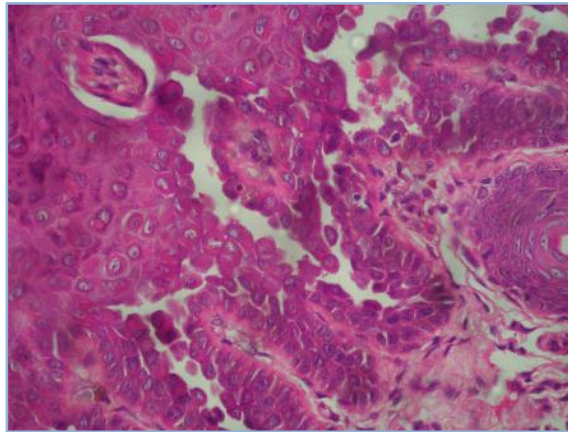


Figure 3b

**DISCUSSION:** Hailey-Hailey disease also known as familial benign chronic pemphigus is a relatively uncommon disease in India. Family history is obtained in about two-thirds of the patients. Incidence is 1 in 50,000 and appears in the third decade of life.<sup>[3,4]</sup> It is rarely found genodermatosis having an autosomal dominant mode of inheritance.<sup>[5]</sup> It was first described in 1939 by dermatologist brothers Hailey and Hailey.<sup>[6]</sup> HHD occurs due to defect in  $\text{Ca}^{2+}/\text{Mn}^{2+}$ -ATPase protein 1 (hSPCA1) due to mutation in ATP2C.<sup>[7]</sup> resulting in lack of  $\text{Ca}^{2+}$ -signaling, irregular sorting and glycosylation of desmosomal proteins in keratinocytes which leads to epidermal defects. Lesions commonly occurs over intertriginous areas such as the neck, axillae, inframammary areas and groin. Generalized or disseminated forms are observed but are extremely rare, usually induced by superficial bacterial skin infection.<sup>[8]</sup> or even rarely drugs.<sup>[9]</sup>

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Lesions are initially flaccid vesicles and papules with erythematous base which may turn into macerated or crusted erosions, have tendency to spread peripherally and turn into chronic, moist, painful, malodorous vegetations with painful fissures. They leave behind postinflammatory hyperpigmentation without scarring. Although mucosal involvement is not common, oral, esophageal, vulvar.<sup>[10]</sup> and conjunctival involvement can occur.<sup>[11]</sup> Longitudinal white lines on the fingernails and fine palmer pits are observed. Atypical variants are hyperkeratotic, verrucous, lichenified, papular, papulovesicular and vesiculopustular forms. Aggravating factors are trauma, heat, sweating, UV light, and infections caused by scabies, bacteria, herpes virus and yeasts.

It has tendency of remission and exacerbations. Rare consequence of HHD is squamous-cell carcinoma.<sup>[12]</sup> The differential diagnoses of Hailey-Hailey disease included fungal infection, intertrigo, psoriasis, extramammary Paget's disease, acanthosis nigricans, pemphigus vegetans and Darier's disease. Histopathology of early lesions shows lacunae formed by suprabasilar clefting with acantholytic cells either singly or in clumps lining the clefts. The lacunae progress to broad, acantholytic vesicles and bullae. Intercellular oedema leads to partial acantholysis and gives rise to areas with characteristic dilapidated brick wall' appearance. Acantholytic, dyskeratotic cells are found within the epidermis.<sup>[13]</sup>

Both of our patients were female. Such female predominance has also been observed by other studies also.<sup>[14]</sup> Family history was positive in case-1 but severity of disease was more in case-2 with early age of onset. It showed that genetic inheritance is not associated with severity. Case 2 presented with verrucous lesions at places which is an unusual morphology.

Topical tacrolimus is found to be effective in HHD.<sup>[15]</sup> The inhibitory effect of calcitriol on T cells and on inflammatory mediators has a role and found to be topically effective. Patients with axillary Hailey-Hailey disease are treated with botulinum toxin type A showed good response.<sup>[16]</sup> Other topical modalities are topical antibiotics, topical steroids, tacalcitol another vitamin D3 derivative and cyclosporine. Systemic treatment includes antibiotics, steroids, cyclosporine, dapsone, methotrexate and thalidomide. In surgical modalities dermabrasion or laser abrasion are effective with long postoperative care. Wide excision and grafting can also be used.

The frequency of exacerbations may be decreased by wearing light weight clothing and avoiding activities that result in sweating or skin friction. Due to its relapsing and remitting course there is a need to have effective treatment options in future to improve quality of life of the patient with Hailey-Hailey disease. Moreover, Hailey-Hailey disease is underestimated. Physicians must keep this disease as a differential diagnosis in resistant intertriginous dermatosis especially when there is a positive family history.

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