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DECEPTIVE PRESENTATION OF FAMILIAL BENIGN CHRONIC PEMPHIGUS – A CASE REPORT

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ABSTRACT
Hailey-Hailey disease is a rare intraepidermal, autosomal dominant, blistering disease. It is characterized by recurrent vesicles and erosions, mostly affecting the neck, groin and axillae. We report a case of Hailey-Hailey disease in a 15 year old female born out of second degree consanguineous marriage who presented with itchy pustules all over the body for duration of two months.

INTRODUCTION

Hailey Hailey disease, a rare autosomal dominant genodermatosis with complete penetrance involving 1in 50000. It is well known since 1939 for its flexural predilection and middle age involvement. The usual clinical picture is that of vesiculopustules and erosions with a positive family history in 60% of the cases.

CASE REPORT

A 15 year old female child born out of second degree consanguineous marriage with normal milestones and regular menstrual cycle presented to our OPD with itchy, raised, red lesions all over the body for duration of two months. Lesions started over the face only to evolve the entire body. Subsequently the patient developed clear fluid filled blisters over the legs which later turned pustular and further ruptured to develop erosions with a foul smell. There was no history suggestive of photosensitivity, fever, bowel disturbances, drug intake, and loss of weight or appetite. There was no history of previous skin lesions.

Mother gave a history of similar evolution of lesions at the age of two, which was then documented as hypozincaemia. Except for a short duration of native treatment, the patient denied any drug intake.

A thorough clinical examination was done. Patient was afebrile. Multiple pustules were seen over face, scalp (Fig 1), neck, hands and a few over abdomen. Erosions and crusting were seen all over body with a predilection for flexures including groin, cubital fossae, popliteal fossae, and finger and toe clefts (Fig 2, 3). Oral examination revealed crusting and erosions over lips and oral candidiasis. Nails and hair were normal.

Our clinical differential diagnosis taking into account the flexural involvement included pemphigus vegetans, pyoderma vegetans or Grover's disease. Whereas predominant pustules with a short history pointed at Acute generalized exanthematous pustulosis and pustular psoriasis. Gram stain from smears taken from pustules showed no organisms or neutrophils. Biopsy was done from lesional site.

To our surprise, histopathological examination showed partial acantholysis with a dilapidated brick wall appearance (Fig 4). Epidermis showed parakeratosis and spongiosis with mild dermal lymphocytic infiltrate. Direct Immuno fluorescence was done in biopsy specimen taken from nonlesional skin adjacent to pustules and erosions. It was negative for IgG, IgM, C1 and C3.

Thus a diagnosis of Familial benign chronic pemphigus was established. The child was started on oral antibiotics and supportives. After the biopsy and DIF reports she was started on oral prednisolone 5mg thrice daily. She has been followed up for 2 months and is presently doing well.

Figure 1. Clinical photograph showing multiple pustules, erosions and crusting over the face and scalp

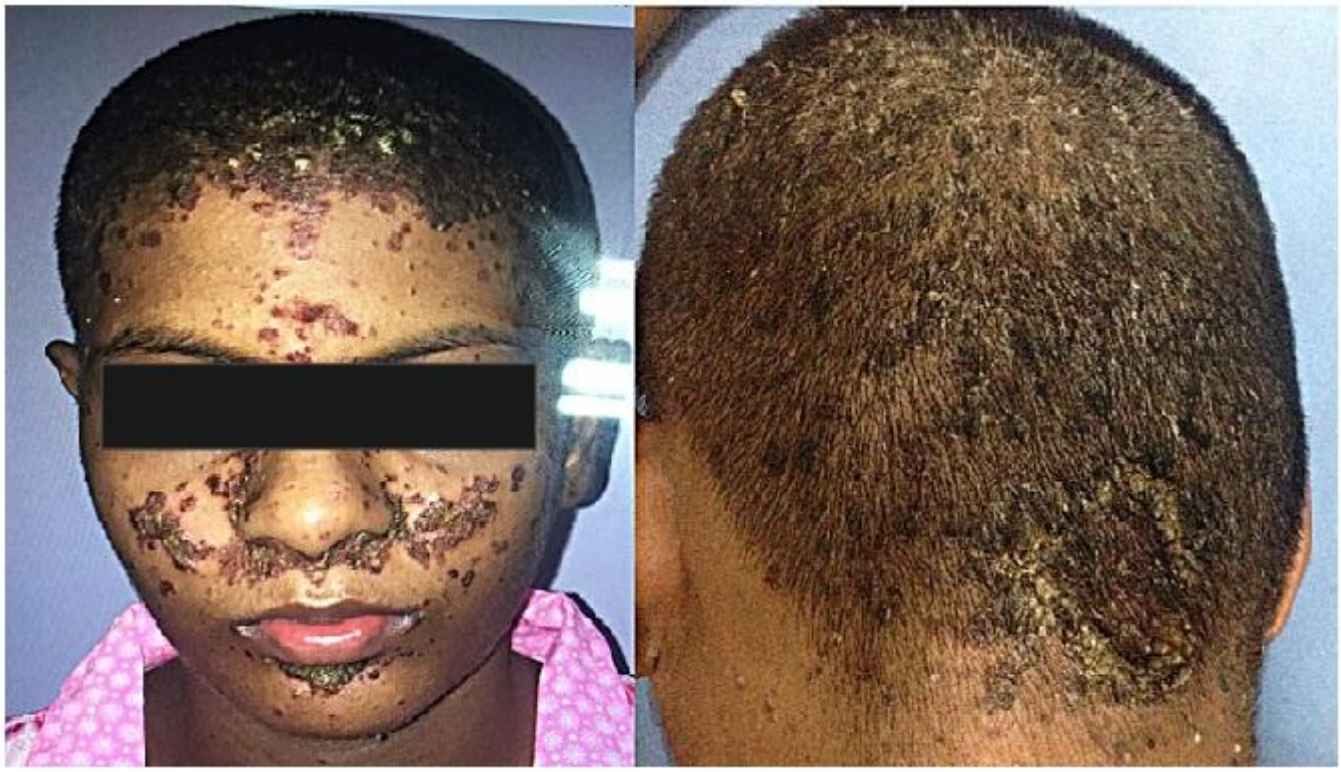


Figure 2. Clinical photograph showing lesions involving the cubital fossae, popliteal fossae and the web spaces of both hands

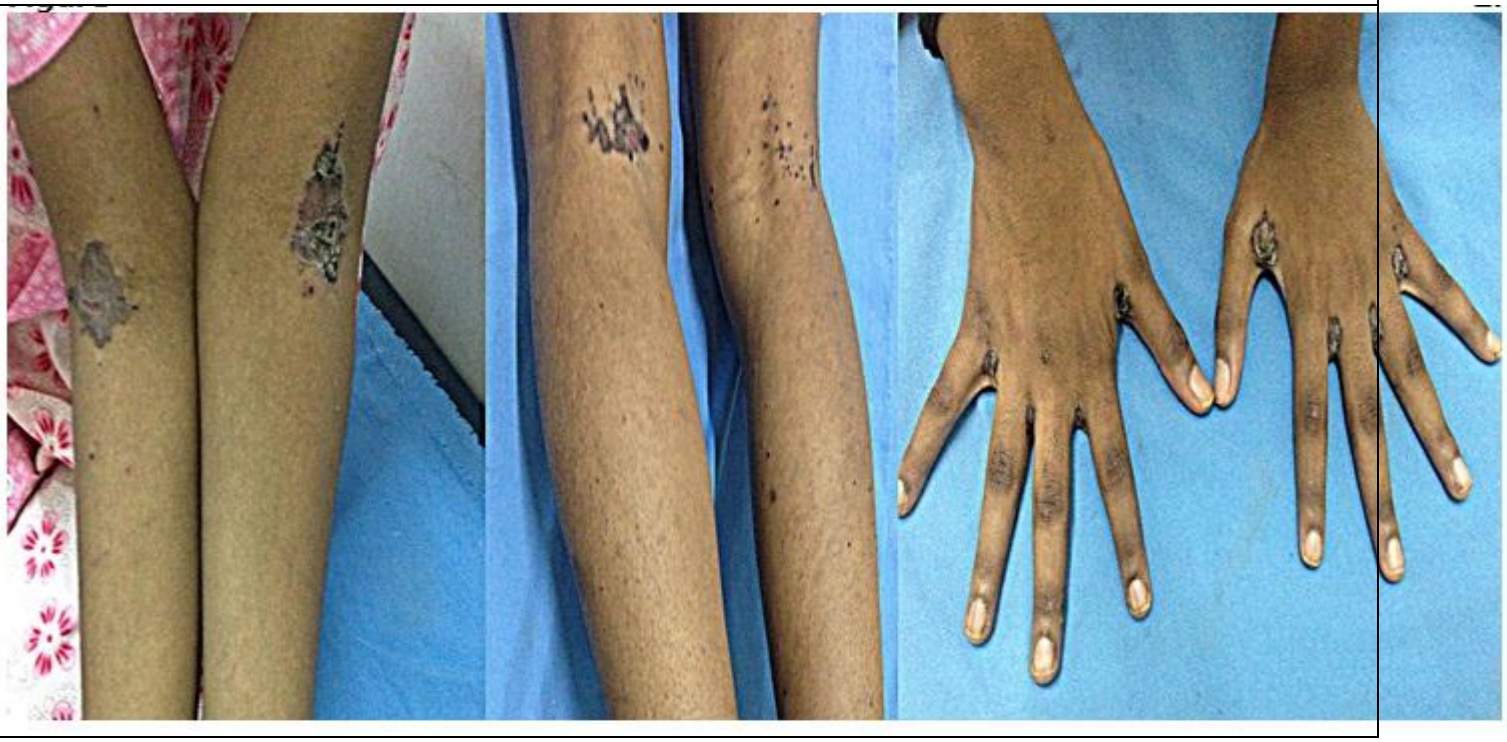


Figure 3. Clinical photograph showing lesions over the dorsum of both feet

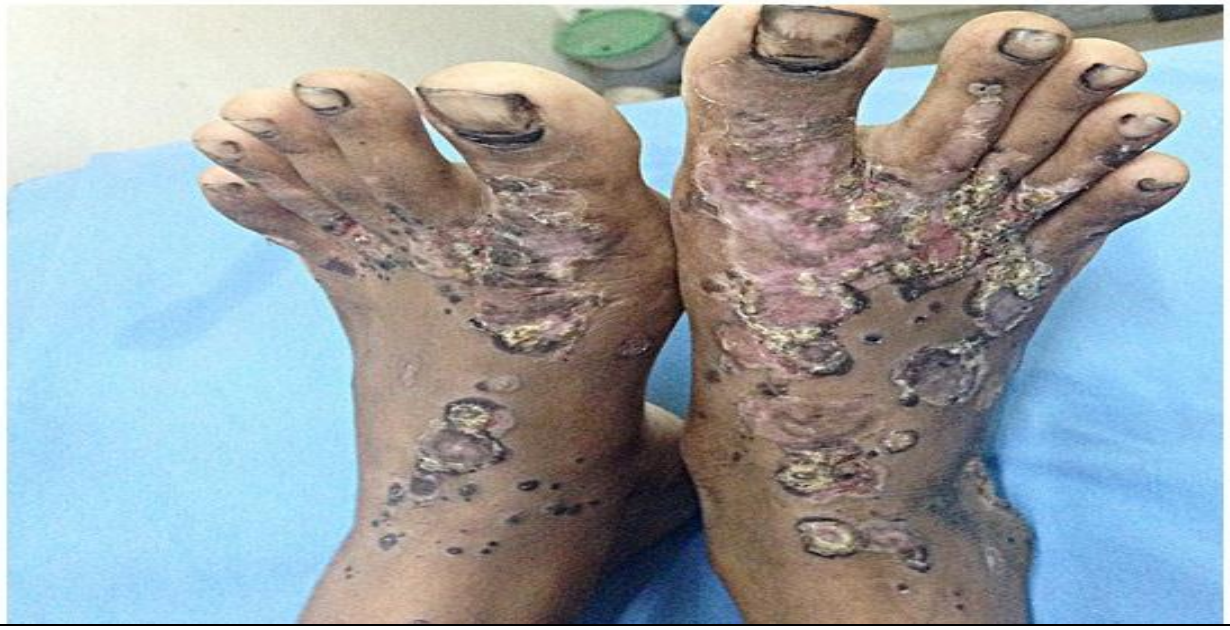
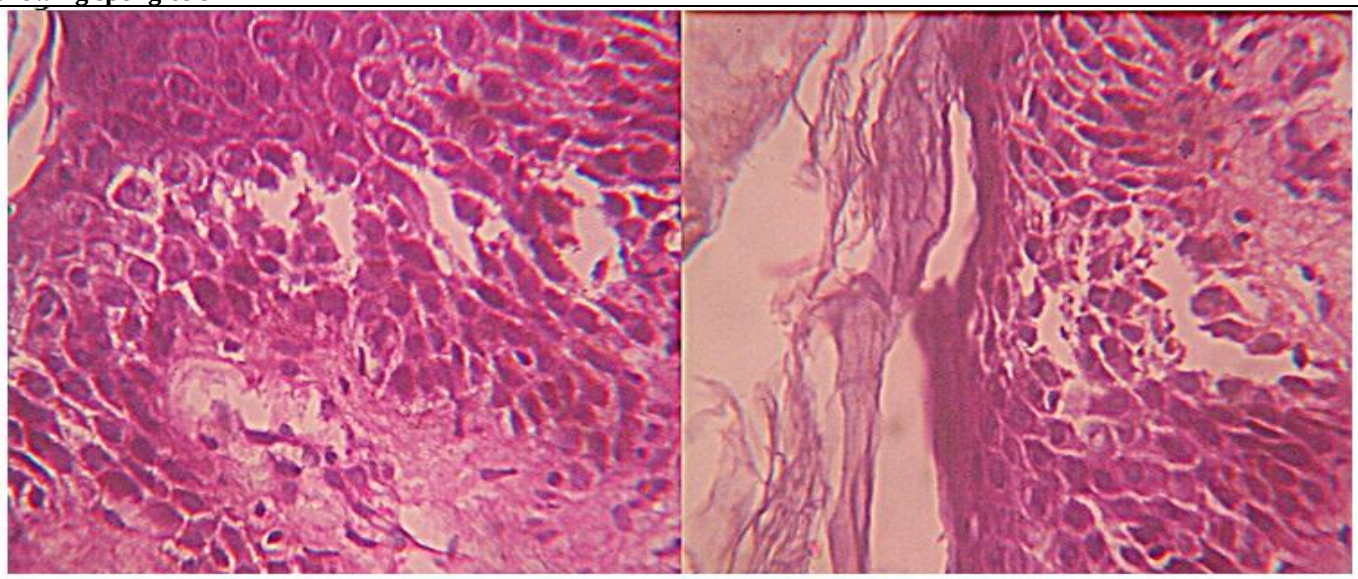


Figure 4. Histopathology showing the partial acantholysis and dilapidated brick wall appearance with epidermis showing spongiosis



DISCUSSION

Howard Hailey and Hugh Hailey were brothers working in Dermatology department in Atlanta, Georgia. They reported recurrent vesiculopustules and erosion involving flexures in two different sets of brothers in 1939 and hence the name [1]. Synonym is Familial benign chronic pemphigus. Pemphigus congenital familial héréditaire' was described 6 years prior to their report by Gougerot and Allee. Though a family history is expected in two third of the cases, there can be mild cases which go unnoticed. The defect lies in ATP2C1 gene encoding $Ca2^{+}$ATPase which lies in Golgi [2,3]. It is involved in calcium and manganese transport and entraps calcium in Golgi. So, defect in this gene depletes calcium in Golgi resulting in the incomplete protein processing and hence defective junctional proteins. The gene defect causes decreased cellular ATP levels which affects the re organization of actin and thus leads to formation of abnormal adherens junction. This explains the pathogenesis of partial acantholysis.

Clinical presentation starts as early as second decade up to fifth decade. The initial lesions of vesiculopustules usually localize in axilla and all other flexures. Generalized cutaneous involvement can also occur apart from the typical flexural involvement [4-6]. Textbook references mention a rarity of involvement of scalp, antecubital and popliteal fossa. The degree of

pruritus and pain may vary with each patient. Evolution of vesicles eroding and further crusting and peripheral extension leads to circinate appearance of lesions with peripheral scaly borders. Malodor, vegetations and fissures occur. The disease may be limited to one or two sites or present rarely as erythroderma. Nail involvement may also occur with longitudinal leukonychia of finger nails. [7] Rare incidence of mucosal involvement especially buccal, conjunctival and vaginal has been documented. Precipitating factors include friction, heat, sweating and UV radiation mimicking Grover's disease. Approximately 17 percent of female patients experience premenstrual worsening of the disease, which suggests that sex hormones may play a role [8,9]. The skin lesions don't leave any sequelae except for a post inflammatory hyperpigmentation.

The course of disease also varies with some patients reporting attenuation of lesions with age. The importance lies in its complications like secondary bacterial, fungal and viral infections including a rare report of Kaposi varicelliform eruption [10]. Its rare co incidence with squamous cell carcinoma may be due to barrier or structural defect leading to infection and activation of oncogenic HPV strains. Two clinical types Segmental Type I and segmental type II has been elucidated. Former due to non mosaic, heterozygous post zygotic mutation and latter due to somatic loss of wild type allele leading to homozygosity [11]. The latter type revealed acantholysis of adnexae in addition, which might be contributing to the recalcitrant nature of disease in some. In these segmental types, patient may develop streaky localized disease.

Histologically, large areas of incomplete acantholysis with a dilapidated brick wall appearance involving suprabasal and intra epidermal area are present. Dyskeratosis with corps ronds and grains is only an occasional feature in Hailey Hailey disease. Protrusion of dermal papillae lined by single layer of basal cells into the acantholytic cavity is named as villi. Chronic lesions show hyperkeratosis and parakeratosis. Moderate superficial dermal lymphocytic infiltrate is also seen. Direct immunofluorescence is negative. Electron microscopy shows a perinuclear tonofilament aggregation.

Differential diagnosis includes Grover's disease, Intertrigo, candidiasis, pemphigus vegetans, inverse psoriasis, eczema, vulvar lichen simplex chronicus and rarely Darriers disease. Histopathological differential diagnosis includes Darriers disease which is excluded by 3 factors namely presence of lacunae, acantholysis more limited to suprabasal area and dyskeratosis more than acanthosis with corps ronds and grains.

Treatment includes symptomatic management, with main stay being topical steroids, rarely intralesional. If recalcitrant and localized, wide excision with grafting has been tried. Newer modalities like CO2 laser, Er YAG laser, photodynamic therapy and dermabrasion play a role. The concept is based on removal of involved epidermis along with its fibroblast. Systemic treatment with oral steroids, retinoids, cyclosporine, methotrexate and dapsone has been documented in few case reports.

CONCLUSION

This case is reported for its rarity in presentation. The usual features like age of presentation, commonest sites of involvement like axilla and submammary area are breached. Our patient with a young age at onset, no recurrent lesions and involvement of rare sites like antecubital fossa, popliteal and web spaces makes this case noteworthy. Also, the pure pustular presentation challenged our clinical acumen. The importance of following up this case in view of prevention of complications and recurrence cannot be overemphasized.

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CONFLICT OF INTEREST:
The authors declare that they have no conflict of interest.

STATEMENT OF HUMAN AND ANIMAL RIGHTS

All procedures performed in human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

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