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Case Report

Exfoliative dermatitis causing diagnostic dilemma: Sibling provides the missing link

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ABSTRACT

A 49-year-old male presented with erythroderma of 3-month duration with a flexural onset. No mucosal lesions were present, and skin biopsy showed features of acantholysis and suprabasal clefting. Direct immunofluorescence test was negative in repeated examinations. The patient was presumptively managed as pemphigus foliaceus with immunomodulators though the level of split was suprabasal rather than subcorneal, and the patient responded well to the treatment. However, his elder sister presented to the department with clinical and histopathological features of classical Hailey–Hailey disease (HHD) which resembled the pathological features found in the index case. This prompted us to review the diagnosis and retrospectively diagnose the index case as HHD presenting with erythroderma.

Keywords: Hailey–Hailey disease, Erythroderma, Exfoliative dermatitis, Siblings

INTRODUCTION

Erythroderma or exfoliative dermatitis is a condition characterized by erythema and scaling involving more than 90% of the body surface area. As the condition is associated with significant morbidity and is potentially fatal even when managed appropriately, it is important to delineate the exact etiology to facilitate precise management. This constitutes a major challenge for the treating physician and a detailed history, thorough clinical examination and investigations including a skin biopsy are often essential for diagnosis. However, a significant proportion of cases remain unclassified or idiopathic even after repeated examinations.[1]

Hailey–Hailey disease (HHD) is a rare, autosomal dominant intraepidermal blistering disorder that is characterized by mutations in the calcium pump gene, ATP2C1. In its classical form, the disease manifests as flaccid vesiculopustules, erosions, fissures, or vegetating lesions in the areas of friction such as neck, axillae, groins, and perineum. It is histologically characterized by loss of adherence between keratinocytes with vesiculation or epidermal clefting. The epidermis shows the characteristic "dilapidated brick wall appearance" which can be attributed to the extensive partial loss of the intercellular bridges between keratinocytes.[2]

CASE REPORT

A 49-year-old male, an office worker, was admitted in our department with generalized erythema and scaling of 3-month duration. He initially noticed reddish lesions over the flexures, which

in a week's time developed into generalized redness and peeling of the skin, starting from the face, progressing throughout the body and associated with generalized edema. There was no history of contact with any potential allergen or any other identifiable triggering factors. The patient was treated with topical azole containing creams and systemic azole antifungals from a local hospital, to which there was no response and the disease progressed to become generalized. He was diagnosed with systemic contact dermatitis (to azoles) at that center and started on treatment with systemic steroids, to which he showed partial response. However, the disease recurred on tapering steroids.

At the time of presentation to our center, there were generalized erythema, fine scaling, and edema [Figure 1]. There were a few erosions and fissures present on the chest, neck, and axillae [Figure 2]. Scalp scaling was also present. Mucosae appeared normal. There were no nail changes. Investigations revealed normal blood counts, elevated inflammatory markers, hypoproteinemia, and dyselectrolytemia. Skin scrapings were negative. There were no features of sepsis, and his blood cultures did not grow any pathogenic organism. Chest radiographs and ultrasonography of the abdomen revealed no abnormalities.

Skin biopsy was performed from the truncal lesions with scaling, which showed psoriasiform dermatitis with spongiosis and foci showing suprabasal clefting, intraepidermal separation, and acantholysis [Figure 3]. In view of the clinical picture of exfoliative dermatitis and the histopathological findings, a diagnosis of pemphigus group of disorders was considered, mainly pemphigus foliaceus, due to the absence of mucosal involvement. The patient was started on high-dose steroids at a dose of 1 mg/kg and immunomodulators (azathioprine 2 mg/kg) along with supportive care, to which there was a satisfactory response. Meanwhile, direct immunofluorescence (DIF) reports were found to be negative on repeated samples, and anti-desmoglein 1 and 3 antibody levels (by enzyme-linked immunosorbent assay) were also found to be normal. The patient was managed in the same line with remission of the lesions, but the diagnosis could not be confirmed; a possibility of pemphigus foliaceus was kept foremost due to the biopsy finding of intraepidermal separation, and DIF negativity and the normal autoantibody titers were attributed to treatment with systemic steroids. Pemphigus vulgaris was considered unlikely due to the absence of mucosal involvement.

His elder sister, a 53-year-old woman, came to our department 3 months later with itchy oozy macerated plaques over the groin [Figure 4]. As she was not responding to antifungals, skin biopsy was done which showed features, resembling her sibling's biopsy findings, but acantholysis was more well-established, giving the characteristic "dilapidated brick wall" appearance, with minimal dyskeratosis [Figure 5]. DIF was negative here as well. With the characteristic clinical picture in the sister, the consistent histopathological findings in both the siblings, and DIF negativity, we diagnosed HHD in both the siblings. Literature search revealed that erythroderma can be a rare presenting feature of HHD, and retrospectively, the

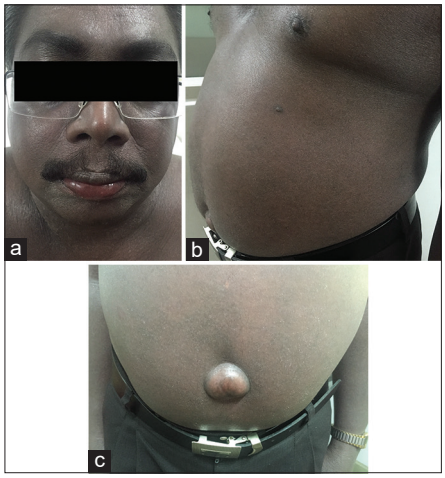

Figure 1: (a) Generalized erythema, edema, and fine scaling over the face. (b) Generalized erythema, edema, and fine scaling over the trunk. (c) Erythroderma with abdominal distension.

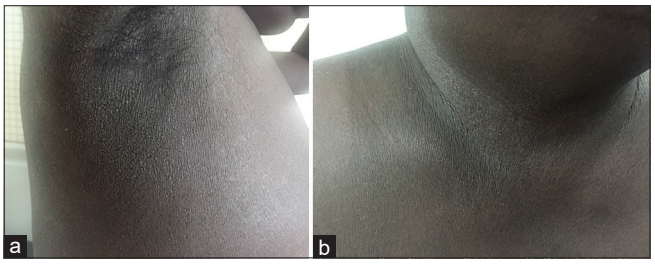

Figure 2: (a) Erosions in the axillae. (b) Erosions in the neck.

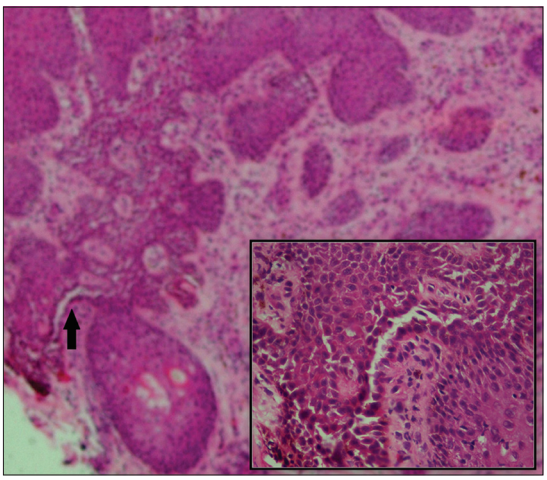

Figure 3: Skin biopsy specimen from the index case showing foci of suprabasal clefting with intraepidermal separation (H and E, ×40) with inset showing high-power view (H and E, ×400).

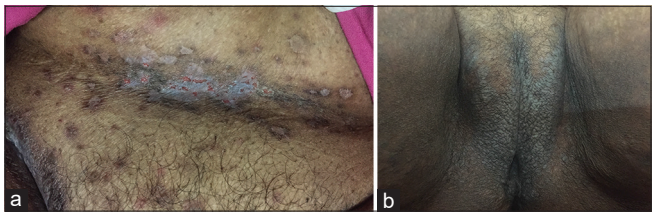

Figure 4: (a) Erosions and fissuring in the lower abdomen. (b) Erosions and fissuring in the inguinal folds.

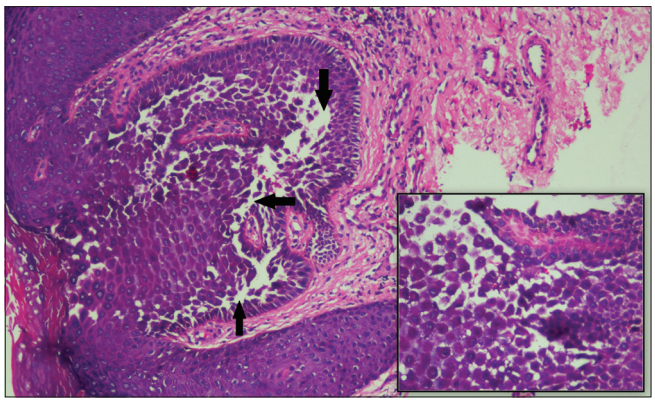

Figure 5: Well-established suprabasal and intraepidermal separation with a "dilapidated brick wall appearance" in the biopsy specimen from the second case (H and E, ×100), inset showing the high-power view (H and E, ×400).

flexural onset of lesions supported this fact. However, genetic studies could not be done due to technical limitations.

The index patient was continued on systemic steroids and azathioprine with slow tapering of prednisolone and with azathioprine being continued at the same dose to maintain the remission. Topical tacrolimus was added for the flexural lesions. The sibling responded well to treatment with topical steroid-antibiotic combination and general supportive measures.

DISCUSSION

Although HHD presenting as exfoliative dermatitis is extremely rare, a literature search has revealed a few prior reports, and Stüttgen has reported three cases of generalized HHD, wherein there was no relevant family history in all three cases.[3] Chave and Milligan have also described a case of acute generalized HHD which initially resembled erythema multiforme or toxic epidermal necrolysis.[4] The important differential diagnoses of HHD include erythrasma, eczema, intertrigo, pemphigus vulgaris, pemphigus foliaceus, Darier's disease, and dermatophytosis. In our case, due to the rare presentation as erythroderma, we had made the probable diagnosis of pemphigus foliaceus; however, in retrospect, the initial presentation as intertrigo, widespread acantholysis in histopathology, and DIF negativity were more suggestive of HHD. The sibling presenting with the classical features helped us to review the diagnosis. Iijima *et al*. have also reported HHD in siblings showing atypical clinical features, but in their cases, the diagnosis was confirmed by genetic analysis, which could not be done in ours due to technical limitations.[5]

CONCLUSION

We report this case as HHD presenting as exfoliative dermatitis is extremely uncommon and can present a diagnostic dilemma. In this particular case, the sibling provided the final and crucial piece for solving this puzzle.

Declaration of patient consent

The authors certify that they have obatined all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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