Hailey-Hailey Disease Masquerading as Intergenerational Candidiasis for 10 Years

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BACKGROUND

Hailey-Hailey disease (HHD), also known as benign familial pemphigus, is a rare genodermatosis first described by the Hailey brothers in 1939. 3 The disease is inherited in an autosomal dominant fashion with complete penetrance but variable phenotypic expression. It can also present as a de novo mutation. Affecting males and females equally, HHD typically presents in the second or third decade of life, with an overall estimated incidence of 1/50,000. 3,4 The disease is caused by a mutation of the ATP2C1 gene, which encodes the ATP-powered calcium pump protein, NSPCC1, in the Golgi apparatus. 5 The impaired calcium pump protein leads to lower calcium levels inside the Golgi apparatus, causing impaired production of calcium binding transmembrane glycoproteins and subsequent loss of cellular adhesion in the stratum spinosum. Histologically, the acantholyis classically seen is often described as having a "dilated brick wall appearance" with the basilar basal layer adherence to the dermis. 6 Other histologic features include intraepidermal vesicles, perineurial eosinophilia, mild dyskeratosis, moderate dermal lymphocytic infiltrate, and variable hyperkeratosis. 7 Direct immunofluorescence studies in the lesion are negative. 8

Hailey-Hailey disease presents as flat vesicles or bullae in intertriginous locations such as the axilla, groin, gluteal, and inframammary folds. These fragile vesicles may rupture and often absent on physical examination. The remaining erosive erythematous plaques commonly present with crusting, maceration, and pruritus. Patients can experience increases in morbidity as affected areas can become painful, pruritic, and malodorous. The disease course fluctuates between episodic remission and exacerbation agitated by friction, heat, sweat, light clothing, increased weight, and infection. 9 Additionally, HHD can be superimposed on the affected areas correlating diagnosis and complicating management of the disease. Longitudinal keratinocytes has been described as approximately 72% of individuals.

CASE PRESENTATION

A 63-year old Hailan female with a past medical history of hypertension and diabetes presented with complaints of painful, irritated rash on her posterior neck, bilateral axilla, intermammary, intergluteal and inguinal folds present for approximately 10 years. Initial treatment included betamethasone cream to affected areas, as well as oral and topical antibiotics, antifungals, and topical corticosteroids for the treatment of intertrigo and candidiasis. The patient reported waxes and wanes of the eruption, occasionally resolving totally, but eventually recurring. She originally denied a family history of skin disorders or cancers. Physical examination revealed violaceous, sharply marginated erythematosus plaques with erosions and maceration located on her posterior neck, bilateral axilla, intermammary folds and groin, with scant surrounding satellite macules. Following years of ineffective treatment for intertrigino-candidiasis, the patient presented to our clinic, and upon further questioning, reported similar eruptions in three of her sisters, as well as her mother.

Suspecting possible Hailey-Hailey disease, a 4-mm punch biopsy was performed in the left axilla. Histopathologic examination revealed a large focus of acantholytic dyskeratotic cells in a "dilated brick wall pattern," with perineural eosinophilia. PAS stain was negative for dermatophytes, and fungal and bacterial cultures performed at time of biopsy were positive for only light growth of Pseudomonas aeruginosa. The patient was treated with appropriate anti-pseudomonal antibiotics. A complete blood count, comprehensive metabolic panel, and lipid panel were ordered in preparation for possible soriatane therapy. She was also significantly improvement in the following year.

CLINICAL DIFFERENTIATION

Table 1. (top right) Treatment and management of HHD

Table 2. (bottom right) Clinical differentiation of intertrigenous dermatitis.

DISCUSSION

The clinical differential diagnosis of Hailey-Hailey disease includes candidiasis, inverse psoriasis, intertrigo, tinea cruris, contact dermatitis, seborrheic dermatitis, hidradenitis suppurativa, and erythrasma. Histologic differential diagnosis includes other intertriginal acantholytic processes such as pemphigus vulgaris, Darier’s disease, and grover’s disease. History and physical examination along with a biopsy help to support the diagnosis. Our case highlights the importance of a proper full history and early biopsy which could have led to an earlier diagnosis.

A fungal infection, such as intertrigious candidiasis, can be separated clinically by the presence of shallow lesions with peripheral papules and pustules. A potassium hydroxide stain will help to confirm the diagnosis but care should be taken as a superimposed fungal infection can often mask underlying Hailey-Hailey disease and lead to a misdiagnosis, as in this case. Inverse psoriasis presents in intertrigenous areas similarly to HHD. The disease presents as erythematous, sharply demarcated, smooth, non-scaly, moist plaques with or without maceration and fissures. Typically patients have a family history of psoriasis and psooriiform lesions with evidence of topical psoriatic nail involvement, including onycholysis and nail pitting. 10

Intertrigo clinically appears very similar to HHD as erythematous plaques with maceration and inflammation of the skin folds. These lesions are prone to bacterial or fungal infections such as candida. A Wood’s light can help to distinguish a pseudomonal infection from a fungus erythrasma caused by C. minutissimum. Pseudomonas fluoresce green under Wood’s light while C. minutissimum fluoresces as coral red patches with well-defined borders. 11

The rash described is distinguished from HHD by the appearance of an annular and axillary active border of pustules or vesicles with either central scale or central clearing in advanced lesions. 12 Tinea cruris may present similarly as well-demarcated erythematous plaques with central clearing and elevated borders that may be active with pustules or vesicles, and may be confirmed by KOH examination.

HHD has no known cure and treatment strategies are aimed at reducing exacerbations and increasing periods of remission. Many treatment modalities have been attempted with most studies demonstrating limited evidence in the literature. Some patients are refractory to treatment, thus individual therapy tailored to each patient is necessary.

General measures should be considered for each patient such as avoidance of hot and humid weather, use of bleach or chlorohexidine baths, weight loss, and use of lightweight loose clothing such as cotton. The use of absorbent pads, barrier and drying agents such as zinc oxide, petrolatum, aluminum sulfate, and talcum powder may be used to keep skin dry and clean. 12,13

First line treatment should consist of a combination of topical antifungals and topical corticosteroids. 13-15 Based on Level IIa and III evidence, clotrimazole should be used for acute flare and topical tacrolimus for maintenance. 16 The topical antifungals that have shown the most success of success include clotrimazole, gentamicin, mupirocin, and ketoconazole. 16,17

Systemic therapy may be necessary if a patient fails the topical antifungal and topical steroid combination therapy. Dapsone has been shown as the most appropriate first line oral therapy with Level Ia and II evidence. 18 Second line oral therapy includes erythromycin, penicillin, and systemic steroids. 17

If a patient is refractory to therapy, additional therapies including surgical excision, botulinum toxin A, dermabrasion, NBI/UV Laser therapy have had limited success. Of these treatment modalities, excision and botulinum toxin A have the highest level of evidence (Level IIa and III) with some evidence showing promise at the present time.

HHD may be difficult to diagnose from other intertrigious diseases. Diagnosis is more difficult if a superimposed bacterial and fungal infection is present.

REFERENCES