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HAILEY HAILEY DISEASE: A CASE REPORT

CHOROBA HAILEY HAILEY: OPIS PRZYPADKU

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Abstract

Hailey Hailey disease or Familial chronic benign pemphigus is a rare autosomal dominant acantholytic disease, clinically characterized by flaccid bullae and erosions in the intertriginous areas, mainly the axillary and inguinal region. We herein report a case of a forty year old female belonging to ethnic Kashmiri population with clinical and histopathological features suggestive of Hailey Hailey disease.

Streszczenie

Choroba Hailey Hailey lub przewlekła rodzinna łagodna pęcherzyca jest rzadką autosomalnie dominującą akantholityczną chorobą, klinicznie charakteryzującą się wiotkimi pęcherzami i nadżerkami w obszarach wyprzeniowych, głównie pach i pachwin. W niniejszym raporcie opisujemy przypadek czterdziestoletniej kobiety należącej do etnicznej ludności Kaszmiru z klinicznymi i histopatologicznymi cechami wskazującymi na chorobę Hailey Hailey.

Key words: pemphigus; acantholysis; Hailey Hailey disease
Słowa klucze: pęcherzyca; akantoliza; choroba Hailey Hailey

Introduction

Hailey Hailey disease is a rare autosomal dominant intraepidermal blistering disorder that is characterized by mutations in the gene that encodes for the golgi-associated Ca2+ ATP ase (ATP 2C1) leading to abnormal intracellular Ca2+ signaling, resulting in acantholysis in stratum spinosum. The condition is clinically characterized by the presence of flaccid vesiculopustules, crusted erosions or expanding circinate plaques in the areas of friction such as neck, axilla, groins and perineum. Flaccid lesions may be hypertrophic and malodorous with soft, flat and moist fissures. Various treatment modalities have been tried for this clinically resistant condition. These include topical agents like corticosteroids, antimicrobials, tacrolimus, calcipotriol and botulinum toxin. Systemic therapy with antimicrobials, retinoids and other immunosuppressive drugs has been tried, but the result with these treatments is not long lasting.

Case Report

A 40-year old female reported to the out-patient department of Dermatology, STD&Leprosy of SMHS Hospital (Associated teaching hospital of Govt. Medical College, Srinagar) with a ten year history of flexural blistering eruption (Fig. 1). The disease started at the age of thirty years with recurrent erythema, vesicles and erosions in the intertriginousareas including axillary, submammary and inguinal regions.These lesions were pruritic and were associated with stinging and burning sensation. These lesions were also malodorous which was a cause of distress for the patient. Recurrent periods of exacerbations of the diseaes were reported especially throughout the summer months. The patient also reported that the eruption would flare around the time of her menstrual periods.

The patient had been treated in the past with both topical and systemic antifungal agents as well as antibiotics but her lesions had been refractory to all kinds of treatment. There was no history of similar complaints in any other family member.

General physical examination of the patient revealed erythematous, macerated plaques with multiple fissures, peripheral vesicles and crusts in the axillary, submammary folds, inguinal and perineal areas. There was no involvement of neck folds and antecubital fossae. There was no involvement of mucous membranes and nails.

All the routine haematological and biochemical investigations were normal.

KOH smear for fungus was negative. Tzanck smear showed a few acantholytic cells. A 4 mm punch biopsy specimen was taken from the affected axillary tissue. It demonstrated intraepidermal acantholysis giving dilapidated brick wall appearance (Fig. 2). Direct immunofluorescense was negative.

With all these clinicopathological findings, a diagnosis of Hailey Hailey disease was entertained in this patient. The patient was put on oral Erythromycin 1 gm daily and topical tacrolimus (0.03%) twice a day to which the patient responded well.

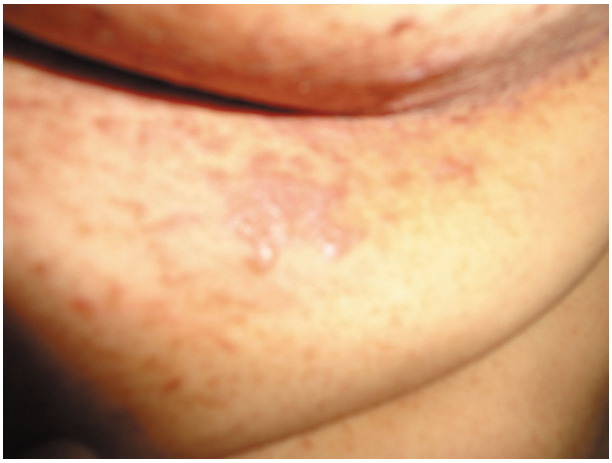

Figure 1. Erythematous macerated plaques with fissures and crusts in the inframammary folds

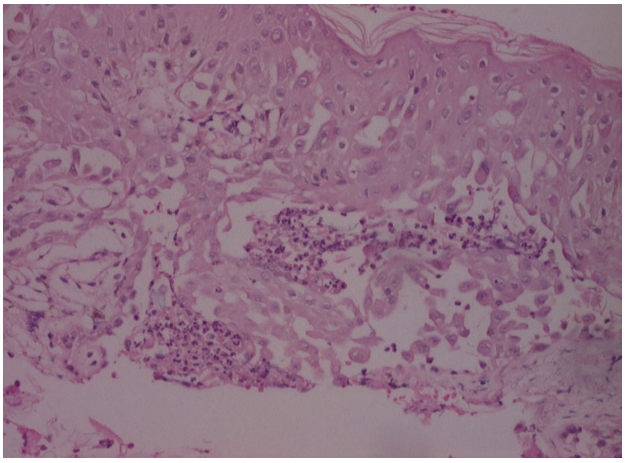

Figure 2. Histopathology showing incomplete suprabasal acantholysis

Discussion

Hailey Hailey disease, also known as familial benign chronic pemphigus was first described in 1939 by the Hailey brothers [1]. It is an autosomal dominant inherited genodermatosis with incomplete penetrance. Family history is obtained in about two-thirds of the patients. The characteristic clinical features are recurrent, fragile, vesicles and erosions in the intertriginous areas (axillary folds, groins, submammary folds and neck folds). Skin lesions mostly present between second to fourth decade of life and can be pruritic, painful and malodorous [2]. Malodorous discharge greatly affects social activity and patient's lifestyle. Recurrent lesions may sometimes lead to restricted mobility. The condition is often debilitating and, both physically and psychologically. Healing occurs without scarring. Longitudinal white bands in the fingernails may sometimes facilitate diagnosis in patients with limited or atypical disease presentations.

Hailey Hailey disease has a variable, usually chronic course, with periods of remissions and exacerbations. The disease can be exacerbated by friction, heat, sweating, physical trauma, infection and stress. Some female patients may experience a premenstrual worsening of their disease, suggesting a role of sex hormones [3].

There are no extracutaneous manifestations and the general health is not impaired. Mucosal involvement is rare, but oral, oesophageal, vulvar and conjuctival involvement has been reported [4].

Hailey Hailey disease is thought to be caused by heterozygous mutations in the ATP 2C1 gene on chromosome 3q 21-q24 which encodes ATPase 1. In affected individuals, reduced activity of this enzyme might cause an instability of the desmosomes, resulting in loss of cohesion between keratinocytes (acantholysis), and development of vesicles. The mechanism by which mutant ATP2C1 causes acantholysis is unknown [5].

Differential diagnosis includes intertrigo, eczema, Darier's disease and pemphigus vegetans. Histopathological examination reveals widespread suprabasal cantholysis with loss of intercellular bridges, which result in 'dilapidated brick wall' appearance. Direct immunofluorescence tests are negative. The treatment of Hailey Hailey disease is very challenging. Patients with Hailey Hailey disease should avoid potential aggravating factors, such as friction and sweating. To help minimize friction, weight should be maintained at appropriate levels and comfortable loose clothing should be worn. Medical line of therapy includes topical corticosteroids, topical antimicrobials, tacrolimus, calcipotriol, tacalcitol and, more recently, botulinum toxin [2,6,7].

Systemic therapy with antimicrobials, retinoids, and immunosuppresants like methotrexate and cyclosporine and dapsone have been tried, but the result with these treatments is not long lasting.

For recalcitrant lesions, wide excision of the involved area with replacement by split graft is widely accepted [8]. Erbium-YAG and CO2 laser ablation have also been reported to be effective [9,10]. Radiotherapy has also been used in local disease control but it does not seem to influence the natural course of the disease [11].

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