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CASE REPORT

Hailey-Hailey Disease Treated Successfully with Acitretin

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Abstract

Hailey-Hailey disease (HHD) is a rare genodermatosis characterized by acantholysis and dyskeratosis of the intertriginous areas. This article presents the case of a 41-year-old Bahraini male, not known to have any medical illness, who presented with a two-year history of bilateral, painful, fissured skin lesions on the groin and axilla. The diagnosis of HHD was confirmed by biopsy. The patient was treated with a course of acitretin 25mg once daily orally for three months, and the treatment led to significant improvement. Up to date, this is the first case to be reported in Bahrain. The case report demonstrated the benefit of using acitretin in the management of HHD.

Keywords: Acantholysis, Acitretin, Axilla, Benign Familial Pemphigus, Groin, Skin Disease

Introduction

Hailey-Hailey disease (HHD), which is also known as familial benign chronic pemphigus is a vesicular and erosive disorder that occurs in the intertriginous areas. The age of onset varies; however, it mainly occurs in early adulthood. It is an autosomal dominant disorder that results from a mutation in the *ATP2C1* gene. This gene provides instructions for producing protein hSPCA1. This protein helps cells in storing calcium. Calcium has a critical role in regulating the cell's proliferation and adhesion. The hSPCA1 protein is essential for the keratinocytes that are located in the epidermis. Therefore, calcium controls the barrier function of the skin and aids in the prevention of bacterial invasion. Mutation in the *ATP2C1* gene reduces the amount of functional hSPCA1 protein which impairs the cells' ability in calcium storage. Abnormal calcium storage affects the function of cells function.

The epidermis becomes brittle and cannot resist even minor trauma because the keratinocytes do not adhere together.[1] The course of the disease is hard to predict; both flares and complete remissions can occur. It usually occurs in the intertriginous areas like armpits, groin, under the breast, and between the buttocks. It rarely occurs in the scalp, antecubital and popliteal fossa, and the trunk.[2] The complications of HHD include predisposition to secondary bacterial, fungal, or viral infections. They might also develop malignant transformation.

People also develop psychosocial issues due to fetid odor and pruritis.[1]

Case Presentation

This is a case of a 41-year-old male patient, without any known medical illness, who presented with a two-year history of bilateral, painful, erythematous, fissured skin lesions on the groin and axilla. It was associated with foul smell, stained his clothes and was painful on movement, which impaired his social and sexual life. These lesions were aggravated by heat and excessive sweating. The patient visited multiple private clinics and was given topical antiseptic and corticosteroids, which did not show any improvement. The patient was not a smoker, and the family and surgical history were insignificant.

On inspection, the lesions were well-demarcated, erythematous, fissured, and peeled 3 x 5cm patch in the right axilla and 2 x 3cm patch in the left axilla with maceration. Along with bilateral well-demarcated, erythematous patch extended over the full inguinal folds (). On palpation, these patches were tender to touch. General physical examination was normal. Respiratory, abdominal, cardiovascular, and neurological examination was unremarkable. Differential diagnosis includes HHD, inverse psoriasis, and pemphigus vegetans. Inverse psoriasis lesions are characterized by a sharper border with fewer erosions and crusts. Pemphigus vegetans usually involve the intertriginous areas. Therefore, considering the patient's clinical presentation, HHD was considered a provisional diagnosis.

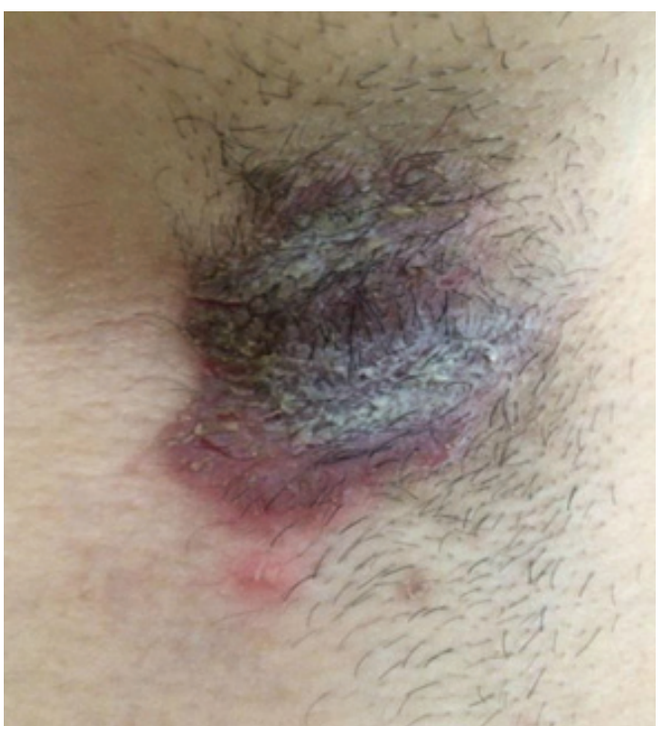

Figure 1: Erythematous eroded plaque with maceration on the axilla prior to the treatment

Upon investigations, the laboratory results were within the normal range. Punched axillary skin biopsy microscopic description showed a parakeratotic, acanthotic epidermis focused on mild supra-basal acantholysis involving the full-thickness of the epidermis with single dyskeratotic cells and mild perivascular lymphocytic infiltrate in the superficial dermis. Special stain Periodic acid-Schiff/periodic acid-Schiff-diastase (PAS/PASD) was negative for fungal organisms (Figure 2).

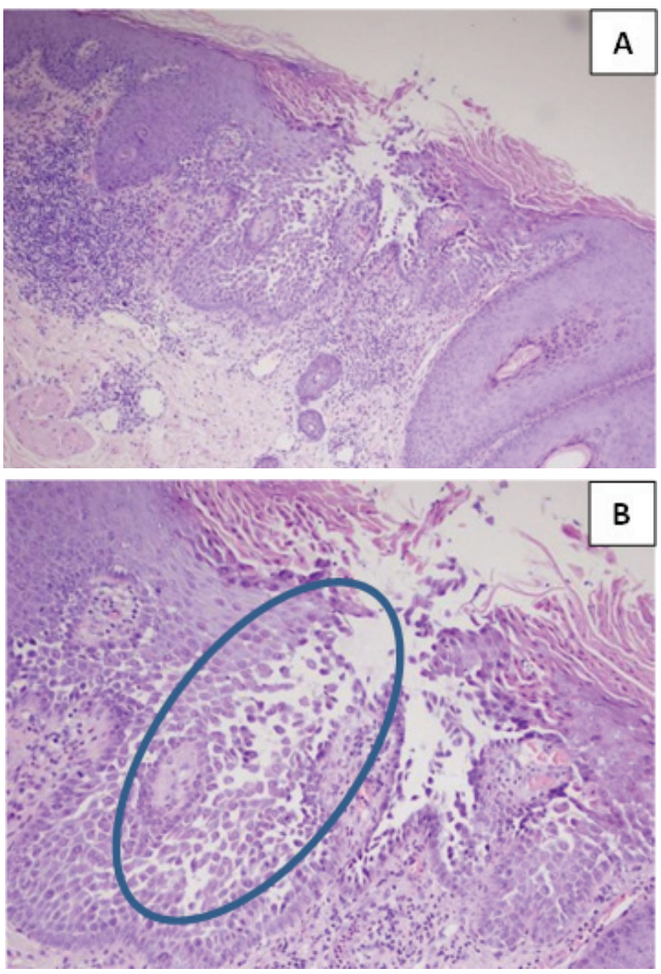

Figure 2: Photomicrographs of skin punch biopsy measuring 1 cm in diameter and 0.3cm in length from the axilla stained with Periodic acid-Schiff/periodic acid-Schiff-diastase (PAS/PASD) consistent with Hailey-Hailey disease (A) Parakeratosis, acanthosis, dyskeratotic cells with suprabasal acantholysis involving the full thickness of the epidermis and mild perivascular lymphocytic infiltrates, (B) Dilapidated brick wall as circled (Hematoxylin & Eosin Stain Objective x10 and Objective x20 respectively).

Based on the microscopic and clinical presentation, the patient was diagnosed with HHD and was prescribed a course of acitretin 25 mg once daily by mouth (OD PO) for three months, antiseptic wash, and topical corticosteroid, which he responded to and showed significant improvement (Figure 3).

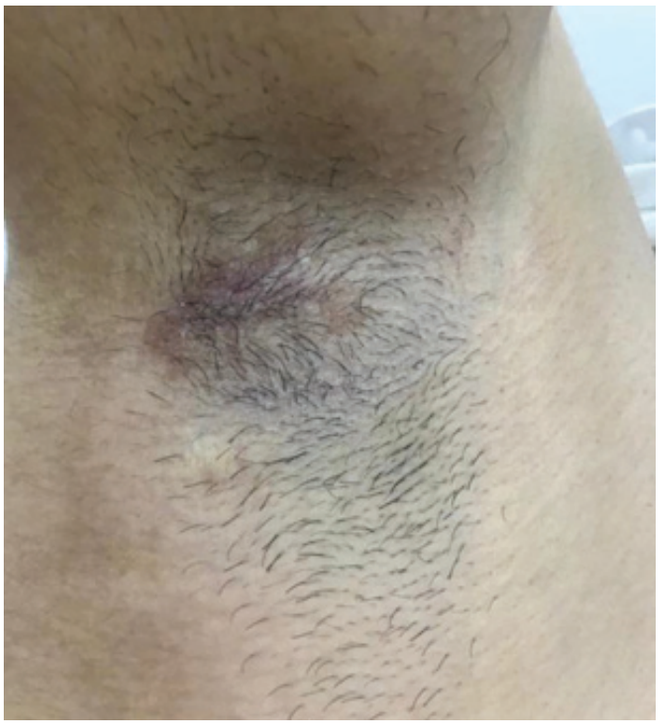

Figure 3: Picture of the axilla after receiving 25mg of acitretin for 3 months

Discussion

HHD is a rare genetic disorder that occurs due to the inability of the skin cells to stick together and lead to the breakdown of the affected skin layers. This occurs because of a mutation in the *ATP2C1* gene. Patients present with vesicles and erosions in the intertriginous areas, mainly the neck, armpits, skin folds, and genitals. These lesions may remit and relapse and heal with post-inflammatory hyperpigmentation (PIH) without leaving scars. Exposure to sunlight and heat, along with perspiration and friction, may aggravate the symptoms. The disorder mostly occurs after puberty, but the symptoms can develop at any age. About 1 in 50,000 people have this disorder, but it is often misdiagnosed or underdiagnosed, so its precise frequency cannot be accurately assessed.[3] The complications of HHD include developing secondary bacterial, fungal, or viral infections that need to be treated with antimicrobial agents. Vegetation and malodorous lesions suggest infection. Recalcitrant intertriginous lesion suggests Herpes Simplex Virus (HSV) infections, and it can be confirmed with direct immunofluorescence (DIF). A few cases with chronic lesions in the anogenital region can develop malignant transformation to squamous cell carcinoma (SCC) and are predisposed to develop infections with oncogenic strains of human papillomavirus (HPV). The management of HHD is challenging. There is no reported cure for this disorder. The treatment mainly aims for symptomatic relief. There is no consensus regarding the best available treatment for this disorder. There are reports of different treatments, but it varies from one patient to another. Topical antibiotics and antifungal agents, along with topical, systemic, and intra- lesional corticosteroids, have shown benefits in many cases. Other treatment options include topical calcineurin inhibitors, topical vitamin D (Calcipotriol), and their combinations, DMARD (disease-modifying anti-rheumatic drugs), which include methotrexate, cyclosporine, dapsone, systemic retinoids, and naltrexone. Botulotoxin A injections are used to reduce sweating, surgical excision, grafting, dermabrasion, and CO2 laser vaporization. Acitretin is a second-generation monoaromatic retinoid. It bindsto receptors present in the nucleus, such as retinoic acid receptor (RAR) and retinoid X receptor (RXR). Therefore, it can normalize the intracellular calcium homeostasis in HHD by exerting its effect on the voltage-gated calcium channels. As a result, it can reduce hyperproliferation, abnormal differentiation of keratinocytes, inflammatory infiltration and induces apoptosis of keratinocytes and lymphocytes.[4] The benefit of using acitretin was shown in two cases of HHD, which were refractory to conservative management.

The first case showed a significant improvement after two months of 10 mg daily acitretin, while the second case showed dramatic response after six months of 25mg acitretin daily.[5,6] This supports our hypothesis that acitretin is effective in treating HHD.

Conclusion

In conclusion, HHD is a rare challenging genodermatosis with no consensus of the best treatment. There are very few cases reported worldwide. This report shares the experience of using acitretin and its benefits in HHD.

Conflict of interest

The authors declare no conflicts among them for this publication

Acknowledgment

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