Hailey- Hailey Disease:- insights from a clinical case

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Key Clinical Message:-

Hailey- Hailey disease is a rare genodermatosis due to mutation in a gene that encodes calcium pumps, required for intracellular calcium homeostasis and transport. It poses a diagnostic dilemma for its rarity and similarity to other flexural skin lesions. This is a case of a 470 year old male with a history of intermittent pruritic lesions affecting flexural areas. We talk about the diagnosis, management and outcome of the case.

Key words:- Genodermatosis, Hailey- Hailey Disease, Calcium Pump, Familial Benign Pemphigus

1. INTRODUCTION:

Hailey-Hailey disease(HHD), also known as familial benign chronic Pemphigus is a rare genodermatosis, which is inherited in an autosomal dominant pattern with variable expressivity[1]. It is characterized by recurrent plaques, vesicles and fissures primarily around the intertriginous areas[2]. Hailey-Hailey disease occurs as a result of mutations in the ATP2C1 gene, which is responsible for encoding intracellular calcium pumps responsible for calcium ion regulation and transport[3].The diagnosis of Hailey- Hailey disease is made through a combination of pertinent history, characteristic clinical morphology and histopathological findings[4]. Here, we report a case of a-47-years old male with HHD affecting intertriginous areas.

2. CASE PRESENTATION:

2.1 History and examination:-

A 47- year-old male presented to the dermatology outpatient department with a 3 year history of pruritic skin lesions affecting bilateral groin areas, scrotum and axilla. The lesion was first noticed by the patient as a black scab accompanied by intense pruritus. The lesions followed a relapsing-remitting course over the period of 3 years, and were found to be aggravated by sweating. No history of similar lesions in the family was noted. Patient was initially misdiagnosed to have an allergic reaction and Levocetrizine was started, which did not resolve his symptoms. Subsequently, he sought advice from another medical center where he was diagnosed to have Tinea with secondary infection and was started on medication. After initiation of medication, slight remission was observed, however he relapsed again after a period of 3 months. Subsequently, a KOH mounted microscopy was done, which revealed no hyphae or spores under the light microscope.

Physical examination revealed excoriated bright red papules on bilateral groin areas, scrotum and perineum (Figure 1), as well as few excoriations around the axilla. There was no scalp, palm, soles or nail involvement. There is no evidence of systemic or mucosal involvement.

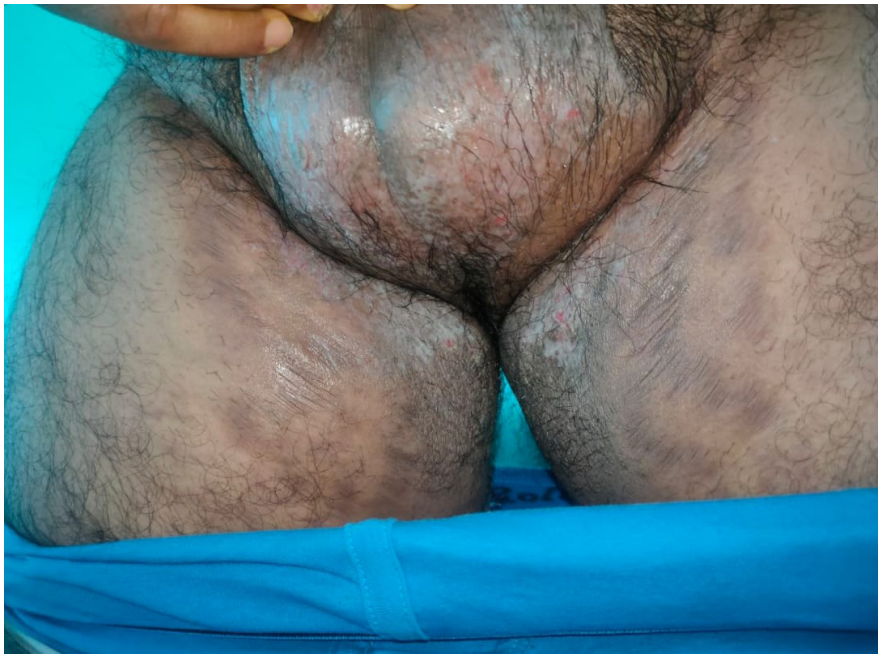

Figure 1 : Macerations and erosions around bilateral scrotal and inguinal areas

Methods:-

Based on the inconclusive findings, a biopsy was performed from the lesion present in the left groin, and the histomorphology was studied, which revealed epidermal hyperplasia and hyperkeratosis along with extensive keratinocyte acantholysis, giving dissipated brick wall appearance, as well as presence of suprabasilar cleft forming vesicles.(Figure 2.A and 2.B).The histomorphological features were found to be consistent with Familial Benign Pemphigus(Hailey-Hailey Disease). Based on clinical as well as histomorphological findings, the patient was diagnosed to have Benign Familial Pemphigus (Hailey-Hailey disease).

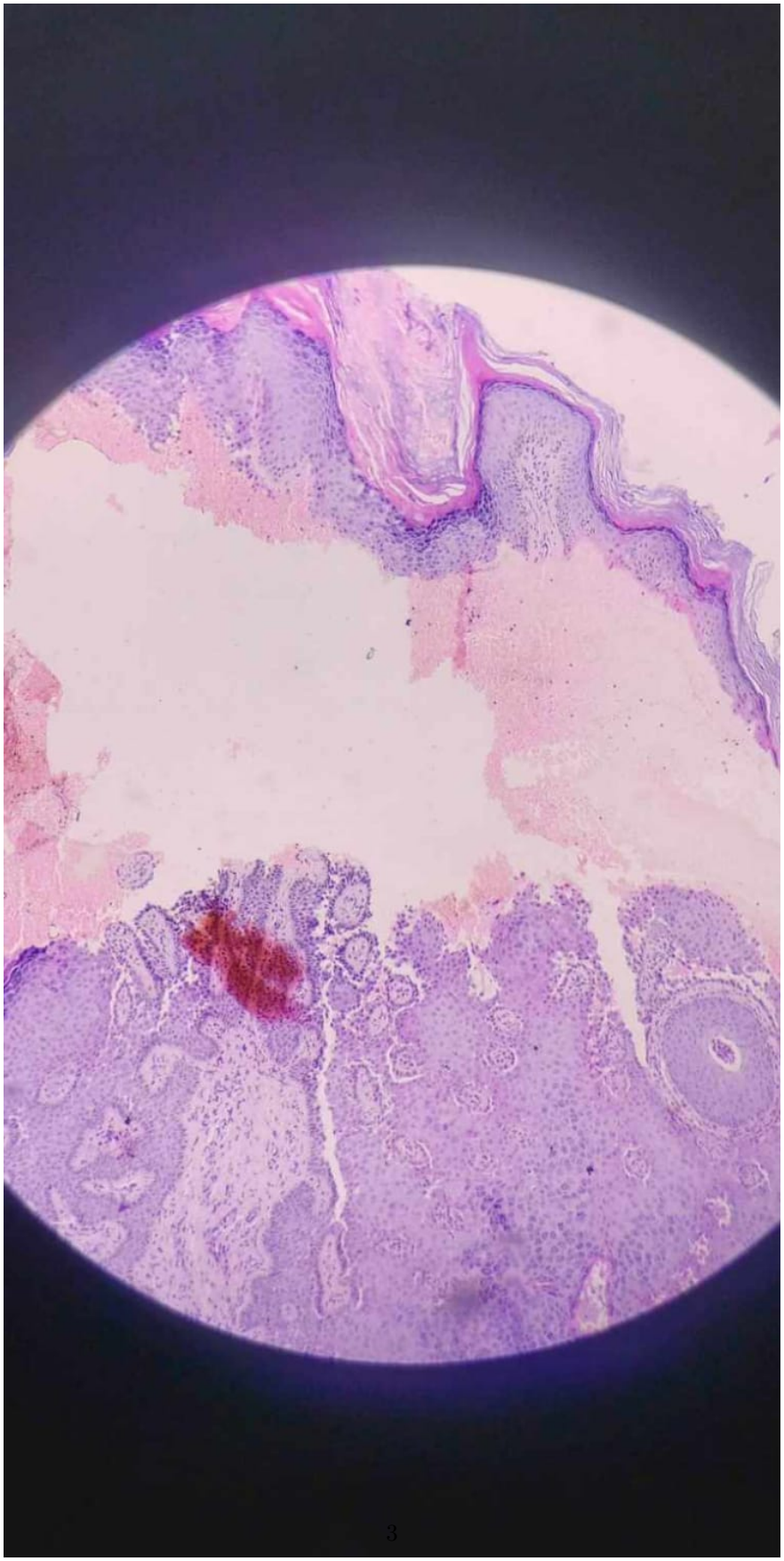

FIGURE-2A :-Histopathology showing extensive acantholysis.

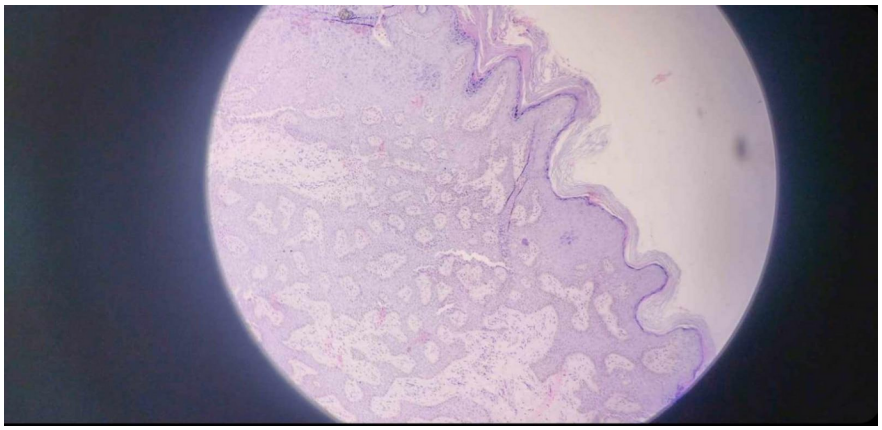

FIGURE-2B- Histopathology showing suprabasilar cleft forming vesicles.

Outcome and Follow up:

He was prescribed topical steroids as well as topical antibiotics. Additionally, he was advised for cold compression and was also advised to wear loose and comfortable clothing. He was also counselled to maintain personal hygiene and avoid heat, sweating and sunburn. On follow up,the patient is under remission and he has been advised for regular follow ups.

DISCUSSION:

Hailey-Hailey Disease(HHD), a relatively uncommon genodermatosis, was described initially by the Hailey Brothers in 1939. It has an estimated incidence of 1 in 50000 with equal predilection towards either sex [1]. It is usually diagnosed after puberty, predominantly in the third and fourth decade of life, however symptoms have been known to develop at any age[5].

Hailey Hailey disease is inherited in an autosomal dominant pattern [1]. It is associated with mutations in the ATPase calcium-transporting type 2C member 1 gene(ATP2C1) gene[3]. The ATP2C1, located on chromosome 3q22 was initially recognized as the causative gene responsible for HHD by two independent studies in 2000 [6,7]. This 27 exon gene is responsible for encoding SPCA1, a secretory pathway Ca2+/Mn2+-ATPase, which is responsible for regulating intracellular Ca2+ homeostasis. Misfolding or downregulation of the SPCA1 protein interferes with Ca2+ sequestration, leading to Ca2+ depletion in the Golgi lumen [8]. Golgi Ca2+ is vital for protein processing, and its depletion may impair the processing of junctional proteins necessary for cell-to-cell adhesion [9].

Hailey-Hailey disease(HHD) commonly presents as flaccid vesicles or bullae, which may progress to crusted erosions and macerations. The most commonly implicated areas are the intertriginous regions [10]. Extracutaneous symptoms are not evident and systemic involvement is not seen. There are rare instances of mucosal involvement, however cases of conjunctival, oral, vulvar and esophageal involvement have been reported [11]. In our study, the patient presented with a history of pruritic skin lesions affecting bilateral groin, scrotum and axilla, primarily affecting intertriginous areas.In addition, no mucosal or systemic symptoms were noted in the patient. HHD is known to have a chronic course with episodes of remission and relapses, and is usually aggravated by mechanical factors such as sweating, heat, infection and friction [12]. In our case, the patient was found to have a relapsing-remitting course of the disease, as well as similar aggravating factors were noted.

Differential diagnosis includes intertrigo, fungal infection, psoriasis, extramammary Paget's disease, acanthosis nigricans, Darier's disease and pemphigus vulgaris [13]. HHD poses a significant diagnostic challenge

to the dermatologist due to its close resemblance to other dermatoses of flexural areas [4]. In our case, the delay in the diagnosis of HHD resulted in a prolonged disease course of 3 years with multiple episodes of relapses.

Diagnosis is usually based on histopathological findings which shows lacunae formed by suprabasal acantholysis, which later progresses to acantholytic vesicles and bullae. A characteristic dilapidated brick wall appearance is often present [14].

There is no specific therapy for HHD therefore, management primarily includes control of aggravating factors, secondary skin infections and cutaneous inflammation. Which includes topical, systemic therapy wide excision of lesion or laser therapy. Topical therapy involves application of antibiotics , steroids, tacrolimus and calcitriol whereas systemic therapy with antibiotics, steroids, methotrexate, tacrolimus, dapsone and thalidomide can be used [15,16,17]. Wide excision of affected area and replacement by split graft can be done for recalcitrant lesions[18]. Erbium-YAG and CO2 laser ablation are other effective treatment options[19,20].

CONCLUSION:

Hailey-Hailey Disease can pose a diagnostic dilemma to a dermatologist, leading to a delayed diagnosis, and imposes a significant effect on the quality of life in the affected patient,., Hailey-Hailey disease might be more prevalent than expected and a positive family history may not always be present. Clinicians should consider HHD as a probable differential while evaluating any patient with flexural skin lesions. Early diagnosis and prompt treatment along with proper counselling can help shorten the course of the disease.

AUTHORS CONTRIBUTION

Prashant Bhatta, Pramod Kumar Kafle, Ramesh Khadayat are involved in conceptualization, resources, writing–original draft, and writing–review and editing. Utsav Dulal and Amrit Bhattarai are involved in conceptualization, investigation, and writing–review and editing. Gaurab Khadka and Sagar Rana Magar are involved in investigation, resources, and writing–review and editing. The manuscript is reviewed and approved by all the authors.

CONFLICT OF INTEREST

None to declare.

CONSENT

Written informed consent was obtained from parents for the publication of these case reports. A copy of the written consent is available for review by the editor in chief of this journal on request.

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