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Case Report:

Hailey-Hailey Disease: An Uncommon Cause of Recurrent Axillary Sinuses

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Abstract: Hailey-Hailey disease is a bullous disorder characterized by the development of flexural erosions, blisters and warty papules. We report the case of a middle aged male presenting with multiple bullae all over the body with discharging sinuses in axilla. Characteristic histopathological findings with negative Immunofluorescence confirmed the diagnosis of Hailey-Hailey disease. This case merits interest because of it's rarity and unusual presentation.

Key Words: Vesiculobullous, Hereditary, Sinus, Histopathology.

Introduction:

Hailey Hailey disease (HHD) is a genetically inherited disease that causes blisters to form on skin although, sporadic cases without any family history are known to exist.[1] It is also known as familial benign chronic pemphigus or familial benign pemphigus and was originally described by Hailey brothers (Hugh Edward and William Edward) in 1939.[2] HHD usually appears in the third or fourth decade, but it can occur at any age and affect people of all races. It then tends to show multiple relapses and remissions throughout life.

Case Report

A 43-year-old man from North India presented with multiple bullae in axilla and groin since 4 months. These were accompanied by red, pruritic lesions in the wrist, forearms and trunk. Patient gave history of scratching after which he developed erosions, most of which healed without scarring. Patient had fluid filled blisters over bilateral lower legs since 10 days. He gave a history of having similar lesions in axilla since 12 years for which he used to take treatment from a local practitioner (antibiotics, corticosteroids and antifungals), obtaining only partial and temporary relief. The lesions aggravated in summer months. No family history suggestive of bullous disorder could be elicited. On examination, there was a discharging sinus in the right axilla surrounded by erythema, scaling and superficial blistering. There was no lymphadenopathy or nail, oral cavity or scalp involvement. Arms and trunk showed few crusted erosions and variably sized bullae with surrounding areas of erythema. He had mild anemia (Hb 10.2g/dl), Differential leukocyte count showed mild neutrophilia (78%) and ESR was elevated (18 mm/Ist hour). Liver, Renal function tests and lipid profile were within normal limits. A clinical diagnosis of Pemphigus vulgaris versus Hailey Hailey disease was made and a biopsy was taken from a recent bulla in axilla. (Figure 1) Histopathology showed epidermal hyperplasia with a suprabasal blister. The bulla was filled with acantholytic cells admixed with neutrophils and serous fluid. A 'tomb-stone' appearance of basal cells was seen and rest of the epidermis showed a "dilapidated brick wall" appearance due to the presence of epidermal acantholytic cells. Dermis was mostly unremarkable. (Photomicrograph 1,2). Direct Immuno-fluorescence (DIF) was negative for immunoreactants , thus confirming a diagnosis of Hailey-Hailey disease. Patient was given oral amoxicillin with oral acitretin 25 mg once daily for 4 months. The lesions started responding within 4 weeks however, complete clearance couldn't be achieved even after completion of treatment. Patient was advised to avoid excessive sweating, friction and trauma.

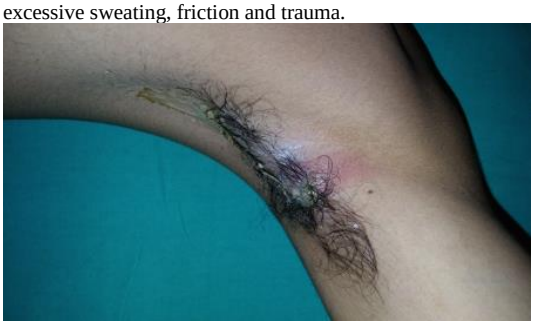
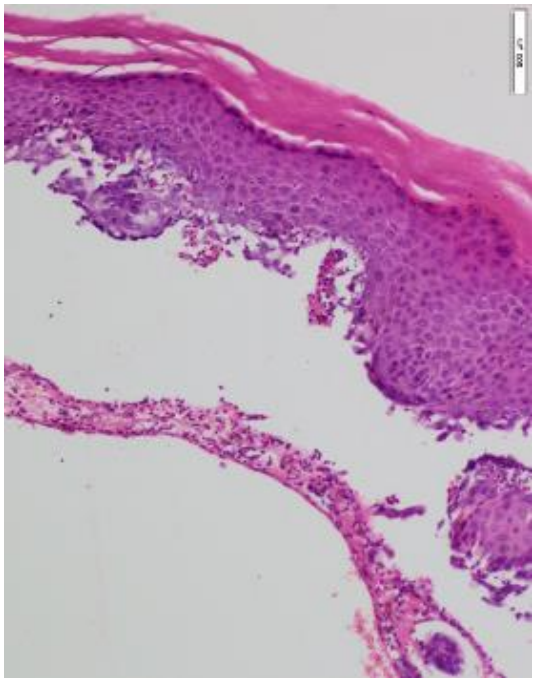
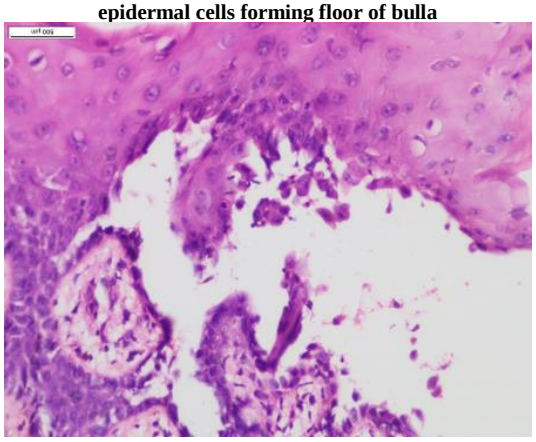


Figure 1: Axillary erythema with ruptured blisters and discharging sinus



Photomicrograph 2: H&E 20x10X Row of basal epidermal cells forming floor of bulla



Photomicrograph 1: H&E 10x10X. Epidermis showing suprabasal clefting with acantholysis giving a "dilapidated brick-wall" appearance

Discussion

Hailey-Hailey disease is a rare autosomal dominant skin disorder with a prevalence of 1:50,000. It usually begins in the third or fourth decade of life. Few sporadic cases arise without a positive family history. Heat, sweating, friction, burns, contact dermatitis and trauma often exacerbates the disease, and most patients have worse symptoms during the summer months.[3] The lesions appear in crops and usually regress in a few weeks, although some lesions follow a chronic course and reappear at the same site.[4] Secondary bacterial infection leading to an unpleasant smell with painful fissures are also common. Herpes simplex can infect blistered sites leading to widespread viral infection (eczema herpeticum). The lesions remain localized to the neck, axillae, and groins in most patients. Other sites which are less commonly involved are the scalp, antecubital or popliteal fossa, and trunk. The defect responsible has now been identified on a gene called ATP2C1 found on chromosome 3q21-24. This gene codes for the protein SPCA1 (Secretory Pathway Calcium/ manganese-ATPase), a calcium and manganese pump leading to abnormal intracellular Ca2+ signalling, resulting in acantholysis in stratum spinosum.[5] The disease has a characteristic histology with layers of acantholytic skin cells lining up like 'a row of tombstones'. The test for antibodies (Direct Immunofluorescence test) is negative in HHD unlike pemphigus vulgaris.

Other conditions manifest microscopic acantholysis within the surface epithelium but are not associated with clinical bullae, such as Darier disease and Grover disease. Bullous Darier's disease can mimic Hailey-Hailey disease very closely, both clinically and histopathologically. Hailey-Hailey disease can be clinically distinguished from bullous Darier's disease by later onset of lesions and rapid appearance and disappearance of lesions with recurrence.[6] Histologically, acantholysis is more incomplete and there are fewer dyskeratotic cells in Hailey-Hailey disease as compared to Darier's disease.

The disease is refractory to most of the existing therapeutic options and relief obtained is usually temporary.[7] The lesions are prone to show exacerbations of lesion or become refractory to treatment when there is secondary co-infection with bacteria, fungi, and viruses. Most patients are managed conservatively with topical corticosteroids as well as topical and oral anti-infective agents with or without surgical excision.[8] The surgical modalities have been reported to be effective, including excision, excision with grafting, dermabrasion, carbon dioxide laser and Er:YAG laser.[9]Scarce reports in the literature describe the use of oral retinoids, tacrolimus or acitretin to manage refractory cases.[10] In 2014, researchers in Italy reported that afamelanotide implants had cleared Hailey-Hailey disease in 2 patients.[11]

Conclusion

Careful correlation of clinical findings with histologic and Immunofluorescence findings usually help to distinguish Hailey Hailey disease from other vesiculobullous disorders

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