International Journal of Research in Dermatology
Sadasivam IP et al. Int J Res Dermatol. 2021 Mar;7(2):285-288
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20210068

Case Series

Hailey Hailey-a blooming disease

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Received: 11 December 2020
Revised: 29 December 2020
Accepted: 07 January 2021

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ABSTRACT

Hailey Hailey disease (HHD) is a rare genetic disorder which is more common in summers. It involves intertriginous areas of the body. Axilla, abdomen, back, nape of neck are the common sites involved. We hereby present three patients of HHD from same geographical area with no blood relation. Two of them had other family members also involved with the similar complaints. One of the patients is 50 years of age. Diagnosis was done both by clinical and histopathological examination. It showed epidermis with intraepidermal bulla and acantholytic keratinocytes giving dilapidated brick wall appearance. Treatment mainly used was topical steroids &antihistamines and patients responded well.

Keywords: Hailey Hailey disease, Familial benign chronic pemphigus, Acantholytic keratinocytes, Acantholysis, Genetic

INTRODUCTION

HHD commonly known as familial benign chronic pemphigus, is a rare autosomal dominant skin disorder.[1] HHD is characterized by mutations in the gene that encodes for the Golgi-associated Ca^{2+} ATPase (ATP 2C1) leading to abnormal intracellular Ca^{2+} signaling, resulting in acantholysis in stratum spinosum.[2] The first onset of HHD generally occurs between 20 and 40 years of age but is uncommon in India(1:50,000).[3,4] It is clinically characterized by recurrent vesicles which rupture, leaving painful fissures and scaly erythematous plaques in the flexures.[5]

This condition with intertriginous area involvement could be easily missed because of its rarity. We are hereby presenting a case series consisting of three case reports of HHD. All of our three patients were residing in the same area but were unrelated to each other and they came to Outpatient department on same day in the month of June 2020. Incidentally after evaluation all of them were found to be having HHD.

This disease could be easily misdiagnosed because of its rarity. HHD was diagnosed both by clinical and histopathological examination. All the three patients showed improvement with regression of lesions but lost for follow-up after three months.

CASE PRESENTATION

Case 1

A 35-year-old married female, residing at Cuddalore (Tamil Nadu) came to the dermatology outpatient department at Aarupadai Veedu medical college and hospital with complaints of itchy fluid filled lesions over the axilla, abdomen, back and groin for four years. Initially started over the axilla but later progressed to involve the groins, umbilicus, back, chest and abdomen. History of similar complaints seen in her daughter.

Patient gives complaints of soaking of clothes with discharge from the lesions. History of increase in lesions during summer and at the time of mensuration present. Patient had taken treatment from many private hospitals which showed no improvements. No history of fever.

On examination patient had multiple hyperpigmented, macerated papules and plaques over an erythematous base involving bilateral axilla, bilateral inframammary areas, abdomen, back, umbilicus, flanks and bilateral groin (Figure 1). Oozing present over bilateral axillae. Few excoriations and crusting seen over the lesions. No involvement of scalp, hairs, nails, mucosa, palms and soles.

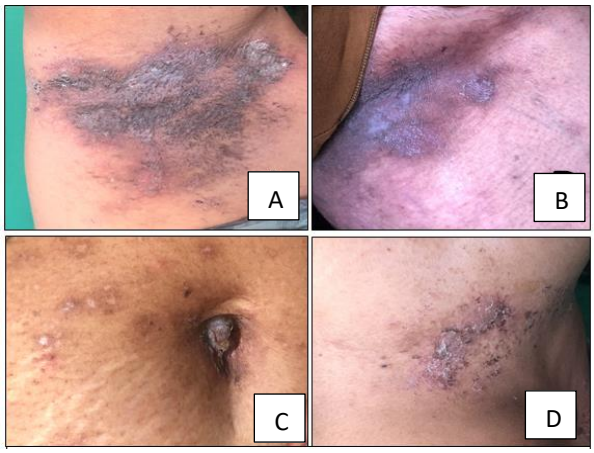

Figure 1: A and B: Macerated, hyperpigmented, papules and plaques over an erythematous base. C and D: hyperpigmented, crusted, scaly plaques.

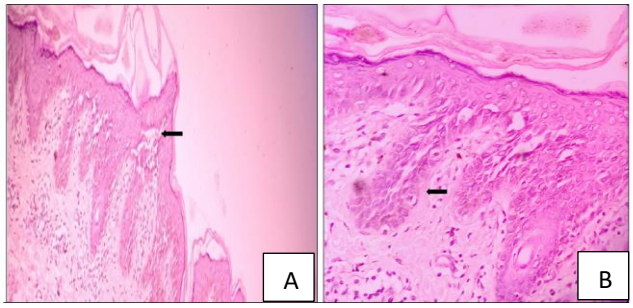

Figure 2: A: Intraepidermal cleft. B: Epidermis of mild acantholytic keratinocytes giving dilapidated brick wall appearance with chronic inflammatory cell infiltrate in dermis.

An elliptical skin biopsy of size 0.5x0.4x0.2 cm was taken with an intact vesicle from the right iliac fossa region. The histopathological examination revealed epidermis showing mild acantholysis mimicking dilapidated brick wall, hyperkeratosis with intraepidermal cleft containing few keratinocytes and few eosinophils. Dermis showed chronic inflammatory cell infiltrates (Figure 2). After routine blood and urine investigations, the patient was started on oral corticosteroid (prednisolone 20 mg) along with oral antihistamines and topical corticosteroid with antibiotic combination.

Case 2

A 40-year-old married female, residing at Cuddalore (Tamil Nadu) came to the dermatology out patient department at Aarupadai Veedu medical college and hospital with complaints of dark, itchy skin lesions over the neck, abdomen and both axilla (on and off) for four years. These lesions started over the neck and gradually progressed to involve the back, abdomen, both legs and axilla. No history of similar complaints in the family members. Patient gave history of getting treatment from a private hospital which showed no improvement. No history of fever, oozing or seasonal variation.

On examination there were multiple excoriated papules and crusted plaques over the neck, B/L axilla, upper back, peri and para-umbilical area, bilateral loin and bilateral popliteal fossa (Figure 3). No involvement of scalp, hairs, nails, mucosa, palms and soles.

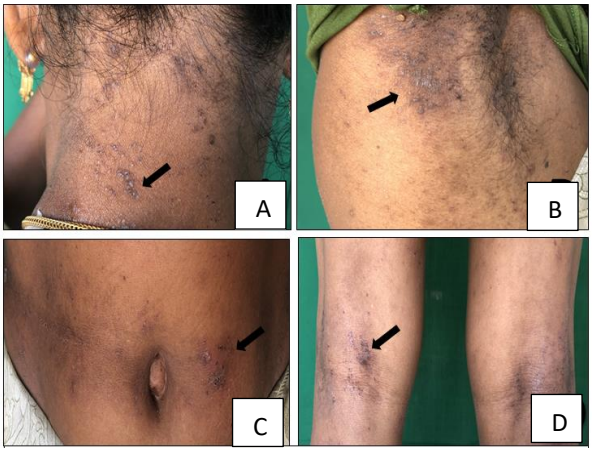

Figure 3: Hyperpigmented, excoriated papules and plaques over nape of neck, right axilla, abdomen, popliteal fossa.

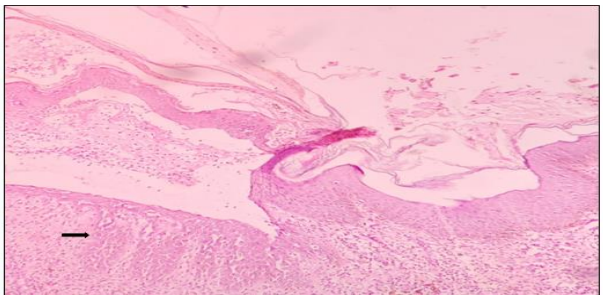

Figure 4: Histopathological image of epidermis with intraepidermal bulla and acantholytic keratinocytes giving dilapidated brick wall appearance. Dermis has inflammatory infiltrate.

An elliptical skin biopsy of size 0.7x0.5x0.3 cm was taken from the upper back and it showed epidermis with

focal ulceration and intraepidermal bulla containing numerous neutrophils and eosinophils. Acantholytic keratinocytes with preserved cytoplasm giving a dilapidated brick wall appearance. Dermis shows numerous neutrophils, lymphocytes and eosinophils (Figure 4). All blood and urine routine investigations were within normal limits. Patient was prescribed with topical corticosteroid with antibiotic combination and antihistamines.

Case 3

A 50-year-old married female, residing at Cuddalore (Tamil Nadu) came to the dermatology outpatient department at AarupadaiVeedu medical college and hospital with history of itchy fluid filled lesions over the abdomen and axilla (on and off) for the past two years. Initially the lesions started over the abdomen and later progressed to involve the axilla and gluteal region. Patient had family history of similar complaints in her daughter (patient was not willing to bring daughter to the hospital as lesions were less). History of aggravation of lesions during last summer. No history of oozing at present. No history of fever.

On examination there was multiple hyperpigmented papules, vesicles and plaques over the bilateral axillary region, umbilicus, left lumbar region and left loin. Few healed areas with post inflammatory hyperpigmentation were seen on the peri-umbilical and axillary regions (Figure 5). Nickolsky sign was positive in this patient. No involvement of scalp, hairs, nails, mucosa, palms and soles.

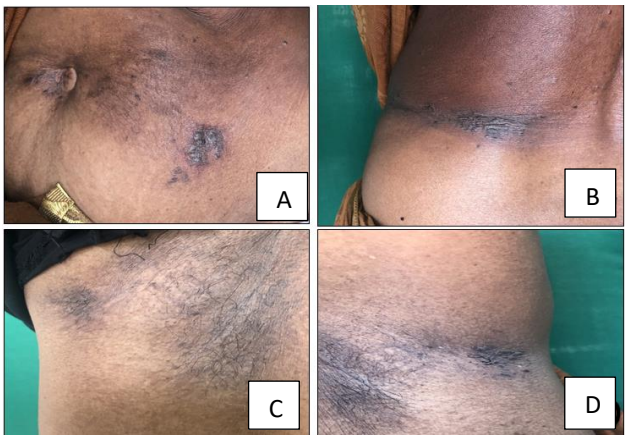

Figure 5: A: Hyperpigmented macules and plaques over left abdomen. Periumbilical post inflammatory hyperpigmentation seen. B: Hyperpigmented papules and plaques over left waist. C and D: Hyperpigmented papules and plaques over both axillae.

Skin biopsy was taken from an intact vesicle of size 0.5x0.3x0.2 cm over the peri-umbilical region and it demonstrated intraepidermal cleft filled with acantholytic keratinocytes showing dilapidated brick wall appearance (Figure 6). All the routine blood and urine investigations were within normal limits. Patient was started on topical corticosteroid and showed improvement.

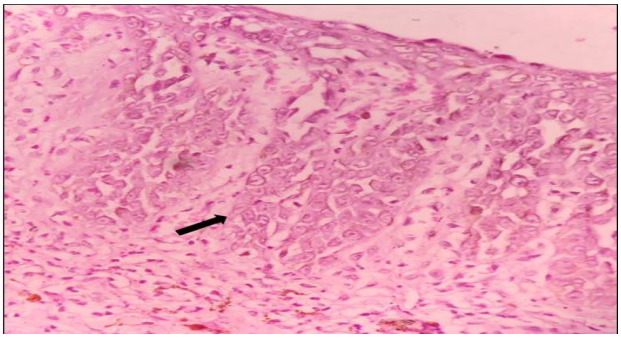

Figure 6: Histopathological images of acantholytic keratinocytes in high power.

DISCUSSION

HHD commonly known as familial benign chronic pemphigus is a rare autosomal dominant skin disorder.[1]About two-third (60%) of patients have a positive family history.[6] In present case series also, family members were affected in case 1 and 3. This correlate and proves the family history in the patients. In our study, axilla, abdomen and waist were involved in case 3, neck, axilla, abdomen and popliteal fossa were involved in case 2, axilla, groin, umbilicus were involved in case 1. Similar area of involvement was seen in the study of Yadav and Sangogram et al.[7,8] The reason for this could be, intertriginous areas have moisture, warmth, there is continuous friction, and there are more chances here to develop bacterial and fungal infections.[9] Oozing of fluid was seen only in first case. There was no involvement of scalp, hair, nails, palms and soles in any of the cases. Similar findings were reported in the study of Prateek, Sangoram, Sharma and Hasan et al.[2,6,8,10] In our case 1, symptoms were aggravated during menstruation. Similar findings were also seen in the study of Hasan et al. The reason for this is not clearly understood. Though more cases are found between 20-40 years, case 3 had 50 years age. Older age involvement was seen in study of Amagai et al (59 years), Malan et al (58 years) and Patel et al.[11-13] For diagnosis histopathological examination was done and it showed epidermis with intraepidermal bulla and acantholytic keratinocytes giving dilapidated brick wall appearance. Dermis had inflammatory infiltrate (Figure 2, 4 and 6). By clinical examination and histopathological findings, we confirmed the diagnosis. Histopathological examination was used in other studies also and by this, diagnosis of HHD was confirmed.[1,2,6-8,10] Fungal infection, intertrigo, psoriasis, extramammary Paget's disease, acanthosis nigricans, pemphigus vulgaris and Darier's disease are some of the dermatosis from which it needs to be differentiated.[6] It is difficult to plan a treatment protocol for HHD. As per the reports, there is no complete cure for HHD.[14] A concoction of topical antibiotics and antifungal agents along with systemic,

topical, and intralesional corticosteroids are useful in the management of HHD in many cases. Tacrolimus was also used in the study of Hasan and Sharma et al.[2,10] Botulinum toxin type A may be an effective and safe nonsurgical alternative for the treatment of HHD in intertriginous areas such as the axillae.[15] Several surgical modalities have been reported to be effective, including excision, excision with grafting, dermabrasion, carbon dioxide laser and Er: YAG laser.[16] The treatment is primarily aimed at symptomatic relief. In our study, we had mainly used topical steroids and antihistamines for the treatment and the patients responded well. One patient required a short course of oral corticosteroids for relief. All the three patients showed improvement with regression of lesions but lost for follow-up after three months.

CONCLUSION

In all the three cases, HHD was diagnosed both by clinical and histopathological examination. All the three patients showed improvement with regression of lesions but lost for follow-up after three months.

Proper diagnosis is extremely important as one of the patients in our case series was taking treatment for four years without any improvement. Any patient presenting with lesions over flexures, a high degree of suspicion of HHD should be kept in mind. Early diagnosis and proper treatment are necessary to prevent the worsening of course of the disease. All the family members have to be screened. Proper counselling is also very important as one of the patients refused to bring her daughter.

Screening has to be conducted in the local community, for presence of similar complaints as all of our three patients were from the same geographical area.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Sadasivam IP, Jagadeeshkumar G, Paquirissamy O, Dileep JE, Takharya R, Dsouza LJ. Hailey Hailey-a blooming disease. Int J Res Dermatol 2021;7:285-8.