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Hailey-Hailey disease: Successful Treatment with Doxycycline

Shivali Kapoor[1], Geetika Vohra[2]

[1]Consultant Pathologist, Dr. Saraswat's Pathology, Kanpur.

[2]Senior Resident, Department of Pathology, Government Medical College, Patiala.

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ABSTRACT

Hailey-Hailey disease is an autosomal dominant disorder which presents with flexural vesicular or verrucous eruptions. Although, there are various medical therapies such as oral and topical steroids, cyclosporine and topical immunomodulators, there is no definitive curative therapy for HHD due to it chronic relapsing-remitting course. We report an Asian female patient with HHD, who responded well with doxycycline. We speculate that doxycycline has potential benefits in providing extended remission period in HHD.

Keywords: Hailey Hailey Disease, Flexural Vesicular or Verrucuous Eruptions, Doxycycline.

INTRODUCTION

Hailey- Hailey disease (HHD) or familial benign chronic pemphigus is a rare autosomal dominant blistering disorder, which commonly affects the flexural areas. The conventional treatment options are topical and oral steroids, topical immunomodulators and vitamin A derivatives. The prognosis with these treatments remain questionable due to the recalcitrant nature of HHD. Recently, therapeutic effects of antibiotics such as erythromycin and doxycycline are investigated. We are reporting, an Asian female patient with HHD, who responded well to doxycycline.

CASE REPORT

A 40-year-old female, presented with an intensely itchy rash under her breasts, axilla and groins [Figure 1]. The rashes were present for nine months. Before visiting our clinic, the rashes were treated as dermatophyte infection, with topical and oral antifungals for four months. She was on oral hypoglycemics for 5 years. On examination, she had multiple hyperkeratotic papules with intense excoriation marks under her breasts, axilla and groins. In some areas, there were flaccid bulla and superficially ruptured skin, demonstrating positive Nikolsky's sign. Skin swabs from the ruptured skin were negative for infection. Tzanck smear from bullous fluid showed occasional acantholytic cells. A skin biopsy was obtained from right mammary and inguinal region. Histologically, there were intraepidermal, suprabasal bullae of varying sizes with many acantholytic cells in the bullous cavity.

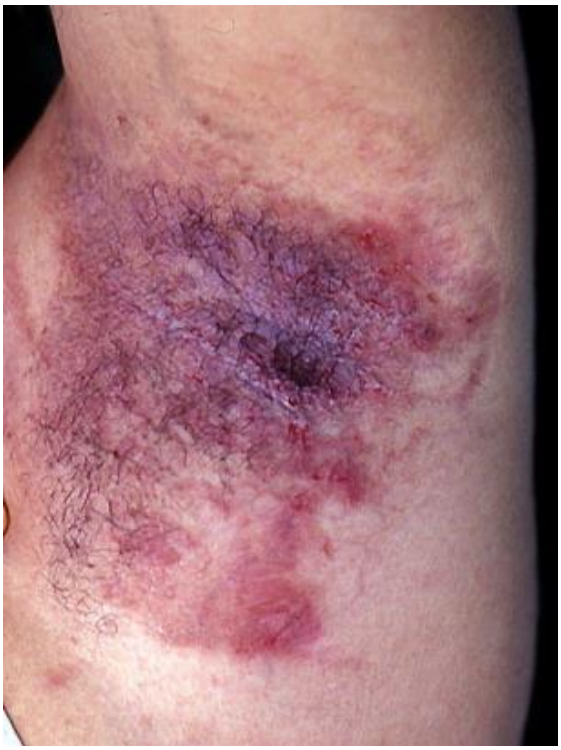

Figure 1: hyperkeratotic papules with intense excoriation marks in axilla

Name & Address of Corresponding Author
Dr. Geetika Vohra,
Senior Resident,
Department of Pathology,
Government Medical College,
Patiala.

There were villi like structures lined with single layer of basal cells, surrounded by loosely cohesive intraepidermal keratinocytes giving the appearance of "dilapidated brick wall", which is characteristic of Hailey Hailey Disease. The direct immunoflorescence did not demonstrate any immune deposits. As she was diabetic, we decided to commence her on oral doxycycline 100mg once daily and topical tacrolimus 0.1% twice daily for a month. The patient noticed good reduction in lesions in the first month. After the second month, the lesions cleared with remnant post-inflammatory pigmentation. The doxycycline and topical tacrolimus was discontinued after 3 months. We followed her up after 4 months of discontinuing the treatment. The patient did not have any recurrence of lesions.

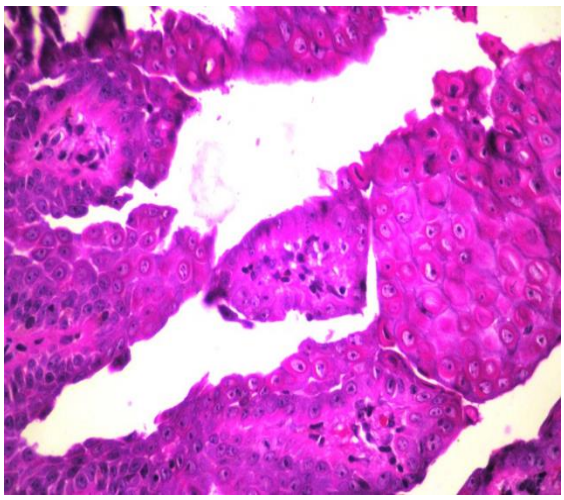

Figure 2: Intraepidermal, suprabasal bullae of varying sizes with many acantholytic cells in bullous cavity.

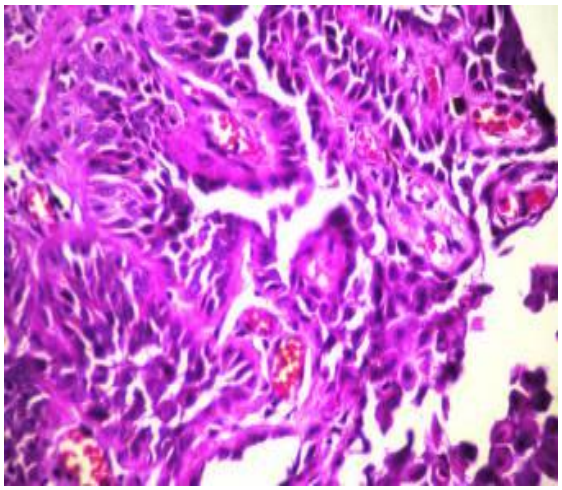

Figure 3: Villi like structures lined with single layer of basal cells, surrounded by loose cohesive intraepidermal keratinocytes giving the appearance of "dilapidated brick wall

DISCUSSION

Hailey Hailey Disease was first described by Hugh and Howard brothers in 1939.[1] It is caused by abnormal protein composition of desmosomal-tonofilament complex in the epidermis, due to mutation in ATP2C1 on chromosone 3q21-24.[2] It is common in 3rd to 4th decade of life with a slight female prepondence. It is commonly characterised by recurrent vesicular eruptions on skin especially in the frictional areas. However, it can also present with crusts, erosions or verrucous papules.[1,2] Oral mucosa involvement is usually rare. Occasionally, the nails can present with longitudinal bands. Heat, sweat, humidity and fungal infections are considered as exacerbating factors for HHD.[1,2] Clinically, it mimics pemphigus vegetans, dariers disease and flexural psoriasis.[1] Histology gives essential evidence to differentiate HHD from other skin diseases. The suprabasal acantholysis with dilapidated brick appearance is characteristic of HHD.[1] HHD affects both psychological and social well-being. Till date, medical therapy used to manage HHD are steroids, topical immunomodulators, cyclosporine and Vitamin A derivatives.[3] Due to the recalcitrant nature of the disease, patients with HHD often require long-term use of aforementioned medications. Ablative methods such as excision with skin grafting,[4] dermabrasion,[5] Co2 laser and Er:YAG laser is reported to be effective in cases of recurrence.[6,7] Due to the chronic course, the vital element in managing HHD is that, the therapy should be well tolerated, safe and cost-effective. A literature search revealed a single case study on six HHD patients treated with doxycycline for 3 months.[8] All six patients had good improvement from 1 week to 3 months of starting the doxycycline. The authors also reported that two patients have had complete remission after more than 5 years of follow-up.[2] Our patient has not had a recurrence after 4 months of stopping doxycycline. We aim to follow-up the patient further, to confirm the effectiveness of the therapy. The exact role of doxycycline in HHD is not known. However, Kobayashi et al, studied the role of matrix metalloproteinase (MMP) and tissue inhibitors of metalloproteinase (TIMP) in HHD.[9] MMP-9 was stained positive in the dyskeratotic cells in HHD.[9] Usage of doxycycline as an effective inhibitor of MMP is widely reported.[10] Thus, we speculate that doxycycline exerts a inhibitor effect on metalloproteinase enzyme, which apparently is a causative factor in HHD. However, until precise information on pathogenesis of HHD is available, the use of doxycycline in HHD remains provisional. The major therapeutic goal in management of HHD is to have a control of lesions and extended remission period with a therapy which is safe and economical. Thus, further insight is required to

understand the effectiveness of doxycycline in HHD, as a monotherapy or as an adjuvant therapy.

CONCLUSION

We speculate that doxycycline has potential benefits in providing extended remission period in HHD.

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