

## Case 4: Benign Familial Pemphigus (Hailey-Hailey Disease)

Dr. C. K. Ho

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### Physical examination

On examination, there were macerated erythematous patches on the neck, antecubital fossa (Figure 1), axilla and groin. In the axilla, small blisters were present. There were superficial erosions with surrounding maceration on the neck. There was no mucosal lesion present.

### CASE SUMMARY

#### History

A 35-year-old female first presented in April 1993 with a 5-year history of recurrent itchy patches affecting the axillae, elbow flexure and neck. The symptoms were exacerbated by hot weather. There was no history of mucosal lesions. Past medical history and drug history were unremarkable. The family history was significant in that both her mother and brother suffered from the same symptoms.

#### Progress

Skin scrapings were positive for fungi and tinea corporis was diagnosed. Topical antifungals were prescribed with a good response. However, over the next six months she presented with recurrent episodes of blisters and erosions affecting the neck and flexural regions. On each occasion she responded to topical antifungals and griseofulvin.

In view of the recurrent nature of the skin condition and positive family history, Hailey-Hailey disease was suspected and a skin biopsy was performed.



Figure 1: Left elbow flexure with macerated erythematous patch

## Investigations

Skin biopsy showed an intra-epidermal vesicle within the basal layer. There was the appearance of a dilapidated brick wall among basal keratinocytes due to partial acantholysis. No corps ronds were present. There were isolated keratinocytes, acantholysis and dyskeratosis of the detached cells. Immunofluorescence was negative. The histological appearance confirmed the diagnosis of Hailey-Hailey disease. Anti-skin antibodies were positive at 1/40 which is low and non-specific. The anti-nuclear factor was negative. Results of complete blood picture, renal and liver function tests were all normal.

## Management

Her condition was controlled on topical steroids and topical antifungals over the next three years. There were episodes of secondary bacterial infection requiring systemic antibiotics. The neck, elbow flexures, groin, vulva and axillae were the main areas affected by blistering and erosions. However the symptoms were mild and did not affect her quality of life.

After diagnosis, she defaulted for two years before presenting again with erosions and blisters in the neck vulva and groin areas. During this period, the symptoms had become less severe and tended to precede menstruation. Her lesions resolved with topical antifungals, topical steroids and oral erythromycin.

## REVIEW ON BENIGN FAMILIAL PEMPHIGUS ( HAILEY-HAILEY DISEASE)

Benign familial pemphigus is a benign disorder characterized by recurrent erosions, blisters and warty papules typically affecting the flexures. It was first described in the Hailey Brothers in 1939. The exact pathogenesis is unknown. It is inherited in an autosomal dominant pattern, with a positive family history in two-thirds of cases. There has been controversy as to whether Hailey-Hailey disease and Darier's disease are separate entities as the two conditions can be similar both clinically and histologically. However, it is now agreed that these are separate conditions.

## Clinical features

The condition usually appears between the third

and fourth decade, and decreases in severity with age. Symptoms are often exacerbated by heat and trauma. The groins, axillae, and neck are the most commonly affected areas. The antecubital fossa, perianal and inframammary areas are less affected. Lesions may also appear on the trunk and in rare cases, affecting the oesophagus, vagina, and larynx.

Infection with bacteria, yeasts, and herpes simplex may precipitate an attack. As the condition responds well to topical antifungals, it is often misdiagnosed as tinea infection. The lesions vary from erosions, blisters, to verrucous plaques. The nails may also be affected with asymptomatic white longitudinal bands (unlike nail changes in Darier's disease which are painful). In a study of 58 cases, Burge found that 46 (79%) complained of itch, while 39 (57%) complained of pain. Out of 27 patients over 50 years old, 17 (63%) experienced less severe symptoms with age, while the disease remained unchanged in seven (26%).<sup>1</sup> Topical steroids and antifungals were effective in controlling the disease.

## Histology

Histologically, there is loss of inter-cellular cohesion with suprabasal acantholysis and the formation of intraepidermal blisters.<sup>2</sup> Elongated papillae, lined by a single layer of basal cells, project into the blister cavity. Not all the desmosomes are lost and the few that remain hold the cells of the epidermis loosely together. This results in the appearance of a dilapidated brick wall." Occasional corps ronds can be found in the granular layer. There is no binding by pemphigus antibodies and minimal inflammation.

## Differential diagnosis

These include pemphigus vulgaris, pemphigus vegetans, Darier's disease, tinea infections, and transient acantholytic dermatosis (Grover's disease).

In pemphigus vulgaris, there is less extensive acantholysis, positive immunofluorescence at the intercellular layers and more degeneration of acantholytic cells within the blister. In cases with vegetative lesions, pemphigus vegetans may be simulated. However, the infrequent occurrence of oral lesions is a distinguishing factor.

In Darier's disease, the seborrheic areas are often affected rather than the intertriginous areas and the

lesions are rarely vesicular. The lesions consist of keratotic or crusted papules and tend to be persistent rather than recurrent. There is also V-shaped scalloping of the nails. In tinea infections, there is no significant family history and, if required, histology will resolve the issue. In Grover's disease, the lesions are self-limiting and may be exacerbated by heat. In rare cases, histology may resemble Hailey-Hailey disease but the changes are more limited and corps ronds and grains are often present.

## Management

In most cases, topical antifungals with or without a topical steroid are effective. For cases with secondary bacterial infection a systemic antibiotic is required. Systemic steroids are reserved for severe exacerbations only, as the disease tends to be benign and the side-effects of steroid therapy outweigh the benefits. In addition, there may be a rebound phenomenon on steroid withdrawal. Cyclosporin has been reported to be effective in isolated cases. Dermabrasion has also been reported to be effective probably by removal of the entire affected epidermis and allowing re-epithelialization from the adnexae.

In a study of eight patients, it was shown that carbon dioxide laser was effective.<sup>3</sup> At 20 months after

treatment recurrence occurred in three patients only. Carbon dioxide laser exerts its effects by causing fibrosis of the papillary dermis without affecting the reticular dermis.

### ***Learning points:***

***Benign familial pemphigus is a benign condition and treatment with topical steroids and/or topical antifungals is often sufficient. Due to its distribution, it is often misdiagnosed as tinea infection. A positive family history is often helpful.***

## References

1. Burge SM. Hailey-Hailey disease: the clinical features, response to treatment and prognosis. *Br J Dermatol* 1992; 126: 275-82.
2. Bruge SM, Millard PR, Wojnarowska F. Hailey-Hailey disease: a widespread abnormality of cell adhesion. *Br J Dermatol* 1991; 124: 329-32.
3. Kartmann M, Reitamo S. Familial benign chronic pemphigus. Treatment with Carbon Dioxide laser. *Arch Dermatol* 1992; 128 (5): 646-8.