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Authors

White, Forrest
Shvartsbeyn, Marianna
Meehan, Shane A
et al.

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Case presentation

Benign familial pemphigus (Hailey-Hailey disease)

Forrest White MD, Marianna Shvartsbeyn MD, Shane A Meehan MD, and Richard W Urbanek MD

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Abstract

A 56-year-old man presented with a 15-year history of scaly red plaques on the trunk and axillae. Skin biopsy was consistent with Hailey-Hailey disease. His condition was refractory to multiple therapies, which included topical and oral antibiotics and topical, intralesional, and oral glucocorticoids. Treatment with subcutaneous botulinum toxin type A at the axillae and on the back led to a nearly complete resolution of plaques in those areas. Botulinum toxin type A should be considered in patients with extensive Hailey-Hailey disease who are fail traditional therapies.

Case synopsis

History: A 56-year-old man with hepatitis B virus infection, hypertension, and hyperlipidemia presented for evaluation of a scaly, red eruption of approximately 15 years duration that had developed on the trunk and axillae. The lesions were pruritic and painful. He previously had been treated with topical glucocorticoids. His father, brother, and sister suffered from the same condition. Shave biopsies were obtained from the right trunk.

The patient was subsequently treated with topical antibiotics, which included clindamycin and mupirocin as well as oral antibiotics, which included trimethoprim-sulfamethoxazole and minocycline. He was also treated with topical glucocorticoids, intralesional triamcinolone and courses of oral prednisone during severe flares. His disease persisted without appreciable improvement.

The patient was then treated with subcutaneous botulinum toxin type A in the axillae, back, and inguinal folds. Following this therapy, he experienced a nearly complete resolution of plaques of the axillae and back.

Physical examination: Large, erythematous, scaly plaques with crusts were present symmetrically on the axillae, inferior aspect of the chest, and superior aspect of the abdomen, posterior aspect of the neck, lower back, and inguinal folds. Some areas were fissured.

Laboratory data: Wound culture grew methicillin-sensitive *Staphylococcus aureus*.

Histopathology: There is intraepidermal vesiculation with acantholysis that involves the spinous layer predominantly. There is a sparse, perivascular, lymphocytic infiltrate.



Figures 1,2. Erythematous, scaly plaques with vesicles and crust

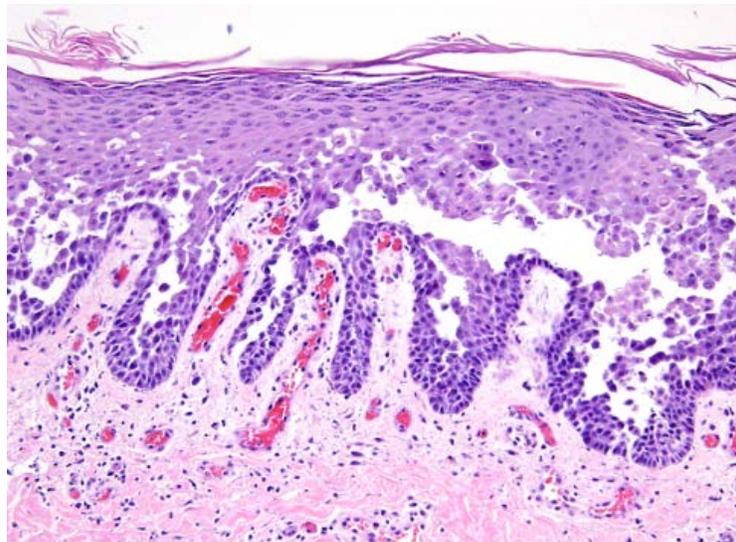


Figure 3. Intraepidermal vesiculation and acantholysis

Discussion

Diagnosis: Benign familial pemphigus (Hailey-Hailey disease)

Comment: Hailey-Hailey disease (HHD), which is also known as benign familial pemphigus, is a rare disorder of epidermal keratinocyte adhesion that was first described by the Hailey brothers in 1939 [1]. HHD is inherited in an autosomal dominant manner and is caused by a heterozygous loss of function mutation of *ATP2C1* gene at 3q22.1, of which over 100 mutations have been described [2,3]. *ATP2C1* encodes human secretory pathway $\text{Ca}^{+2}/\text{Mn}^{+2}$ -ATPase protein 1 (hSPCA1), which pumps Ca^{+2} across Golgi membranes. It is felt that defective pump function leads to disruption of cellular connections, which results in acantholysis. Clinically, HHD appears as symmetric, erythematous plaques that often involve the axillae, inguinal folds, and other flexural areas, which may develop erosions and fissures and are susceptible to superinfection.

There is no standard therapy for HHD. Excess heat, moisture, and friction, which have been shown to exacerbate the disease, should be avoided. Commonly used topical agents include topical antibiotics, topical glucocorticoids, and topical calcineurin inhibitors. Systemic therapies used in the treatment of HHD have included oral antibiotics, cyclosporine, methotrexate, acitretin, and alefacept. In addition, destructive therapies such as surgical excision, dermabrasion, and laser treatment have been employed.

Botulinum toxin, which is derived from the bacterium *Clostridium botulinum*, blocks neuromuscular transmission by inhibiting the release of acetylcholine. Botulinum toxin type A is used in the treatment of hyperhidrosis, with effects lasting an average of three to 14 months [4]. Botulinum toxin has been reported as an effective therapy in HHD, with partial to complete resolution of lesions reported in small number of patients [5-9]. The anhidrotic effect of botulinum toxin may lead to less physical irritation of HHD lesions as well as reduce colonization and superinfection of disease plaques.

Our patient received a series of subcutaneous injections of botulinum toxin type A in the axillae, back, and inguinal folds. The axillae were injected four times, with injections spaced four to seven months apart. The back was injected twice, with four months between injections. The inguinal folds were injected five times, with injections spaced two to seven months apart. Treatment with botulinum toxin led to a nearly complete resolution of plaques of the axillae and back. Our patient adds to the small literature base that describes successful response to botulinum toxin therapy in HHD.

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