

CASE REPORT

A Case of Eczema Herpeticum with Hailey-Hailey Disease

Gun Hong Lee, M.D., Yun Mi Kim, M.D., Sung Yul Lee, M.D., Jong Suk Lee, M.D.,
Young Lip Park, M.D., Kyu Uang Whang, M.D.

Department of Dermatology, Soonchunhyang University College of Medicine, Seoul, Korea

Eczema herpeticum is the dissemination of herpes simplex virus in the setting of a preexisting skin disease. Hailey-Hailey disease [familial benign chronic pemphigus] is a blistering dermatosis that is inherited as an autosomal dominant trait and it usually presents itself around the third or fourth decades. Coexistence of eczema herpeticum and Hailey-Hailey disease is an infrequent occurrence. Four such cases have been reported in the English and German medical literature. We report here on an unusual case of eczema herpeticum that coexisted with Hailey-Hailey disease in a 47 years old man and we review the relevant literatures. (**Ann Dermatol 21(3) 311~314, 2009**)

-Keywords-

Eczema herpeticum, Hailey-Hailey disease

INTRODUCTION

Eczema herpeticum is also known as Kaposi's varicelliform eruption, and this refers to a herpetic superinfection of a pre-existing skin disease. There have been reports of eczema herpeticum occurring in atopic dermatitis, dyskeratosis follicularis, Darier's disease^{1,2}, pemphigus foliaceus³, mycosis fungoides, ichthyosis vulgaris, Hailey-Hailey disease⁴⁻⁷, Sézary syndrome⁸ and in patients with burns⁹. When eczema herpeticum is recognized early, it is easily and effectively treated with antiviral agents. Hailey-Hailey disease is a blistering dermatosis that is

inherited as an autosomal dominant trait and it usually presents around the third and fourth decades. This disease is characterized by recurrent eruptions, usually on the intertriginous areas, i.e., the axillae, the groin and/or on the neck. Vesicles, erosions and crusts may be present in these erythematous lesions. A decreased numbers of desmosomes have been implicated in the pathogenesis of Hailey-Hailey disease. The therapeutic options for this disease are limited.

The occurrence of eczema herpeticum together with Hailey-Hailey disease is rare. There is little information linking herpes simplex virus with the exacerbation of Hailey-Hailey disease. Only four such cases have been reported in the English and German medical literature. To the best of our knowledge, this is first such case report in Korea. This report describes eczema herpeticum in a patient with Hailey-Hailey disease, and this was confirmed by skin biopsy and the clinical features.



Fig. 1. Multiple umbilicated vesicles on the chin.

Received November 17, 2008, Accepted for publication February 22, 2009

Reprint request to: Sung Yul Lee, M.D., Department of Dermatology, College of Medicine, Soonchunhyang University, 23-20, Bongmyeong-dong, Cheonan 330-721, Korea. Tel: 82-41-570-2270, Fax: 82-41-578-2270, E-mail: dermsung@schca.ac.kr

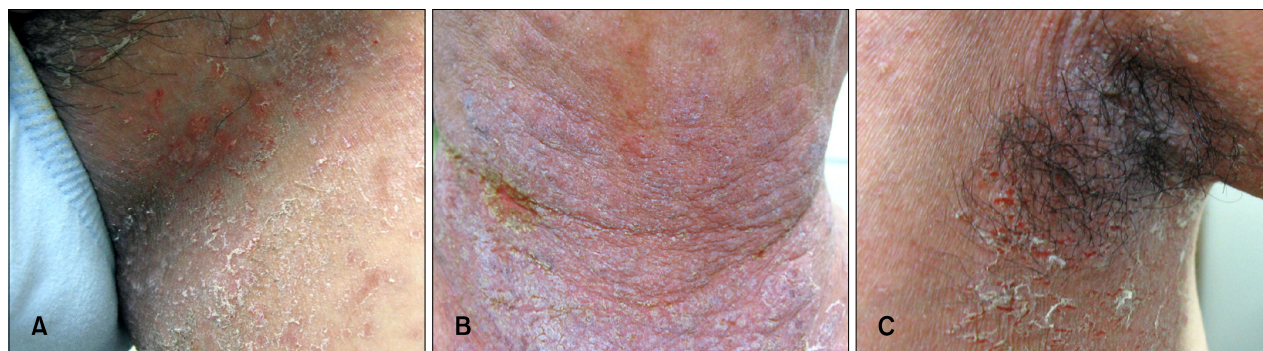


Fig. 2. Erythematous scaly plaque with maceration of the inguinal area (A), the nape of the neck (B) and the axilla (C).

CASE REPORT

A 47 years old man visited our Department of Dermatology with a presentation of painful vesicles on the chin and he'd had these lesions for the previous 10 days (Fig. 1). The multiple umbilicated vesicles on the chin were suspected to be eczema herpeticum according to the clinical features. This man had also presented with a painful, erythematous, fissured plaque involving the flexural areas for the previous year (Fig. 2). He complained of an unpleasant smell from his lesions. Physical examination revealed recurrent painful erosions, vesicopustules and scaly erythematous plaques in the intertriginous areas, i.e., the axilla, inguinal folds and the neck. The lesions were intermittently aggravated and especially during the summer, which restricted his mobility. The bullous and erosive lesions epithelized slowly without leaving scars. He has a medical history of diabetes and hypertension.

The KOH mount was negative. The abnormal laboratory test results included an elevated total white blood cell count of $19,740 \text{ cells/mm}^3$. Other investigations, including blood sugar, urinalysis, liver function tests and serological tests for syphilis, were within the normal limits. Serology for IgM and IgG antibodies to herpes simplex was not performed.

A biopsy specimen from an active skin lesion on the chin showed marked infiltration of the chronic inflammatory cells in the dermis. Inclusion bodies were not seen. The skin biopsy from the right groin confirmed the diagnosis of Hailey-Hailey disease. It showed focal hyperkeratosis and dyskeratotic cells similar to corps ronds within the granular layer. A cleft was present within the epidermis, and the epithelium beneath the cleft showed partial acantholysis. Suprabasal bulla and the appearance of a dilapidated brick wall in the epidermis were seen (Fig. 3). So, we diagnosed this case as eczema herpeticum with

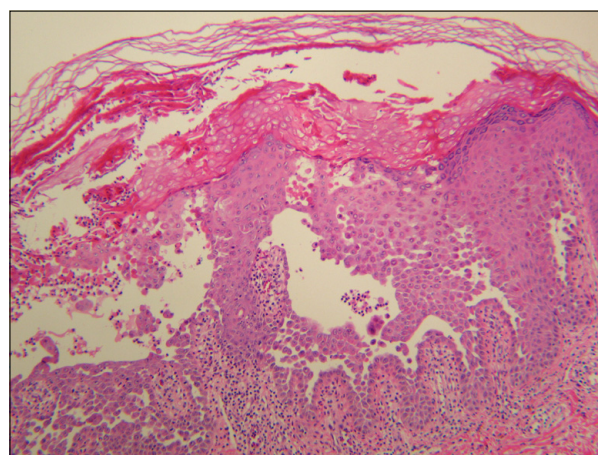


Fig. 3. Intraepidermal clefts suprabasally in the epidermis and the characteristic acantholysis with the appearance of a "dilapidated brick wall" (H&E stain, $\times 100$).

Hailey-Hailey disease.

He was treated by a combination of systemic antibiotics and oral famciclovir, topical pimecrolimus and wet dressing. The vesicles on the chin were rapidly controlled by antiviral therapy within a week. But during the usage of topical pimecrolimus, the patient complained of local irritation, and then this medication was changed to topical steroid cream. After these treatments, slight improvement of his Hailey-Hailey disease lesions was noted.

DISCUSSION

Eczema herpeticum is a potentially life-threatening viral infection that arises in pre-existing skin conditions. In some cases, it may progress to a fulminating, life-threatening infection and it can have severe sequelae, including herpes keratitis, disseminated infection with visceral involvement and death. It begins as clusters of umbilicated vesiculopustules in the areas where the skin

has been affected by a preexisting dermatitis.

Disruption of the stratum corneum secondary to skin disease is the most common predisposing factor¹⁰. There have been reports of eczema herpeticum occurring in atopic dermatitis, Darier's disease^{1,2}, pemphigus foliaceus³, pemphigus vulgaris, pityriasis rubra pilaris, Hailey-Hailey disease^{4,7}, irritant contact dermatitis, cutaneous T cell lymphoma, seborrheic dermatitis⁸, Wiskott-Aldrich syndrome⁸, congenital ichthyosiform erythroderma and Sézary syndrome⁸. Eczema herpeticum may also occur when there has been recent injury to the skin such as second-degree burns⁹, autografted skin and post dermabrasion. A commonality among all these diseases is the disruption of the integrity of the epidermis.

Viral cultures of fresh vesicular fluid and the direct observation of the infected cells scraped from the ulcerative lesions by direct fluorescent antibody (DFA) staining are the most useful and reliable diagnostic tests available^{10,11}. A Tzanck smear of an opened vesicle or erosion can provide a rapid diagnosis when it shows the characteristic epithelial multinucleated giant cells and acantholysis. If the lesions are atypical, equivocal or old, then biopsy or the polymerase chain reaction (PCR) should be considered.

Therapy should be instituted without delay when there is a high suspicion or a positive Tzanck preparation. The early use of both antiviral drugs and antibiotics is extremely important; their use should not be delayed pending laboratory tests. The most commonly used antiviral drugs are the nucleoside analogs, which inhibit viral DNA polymerase. The initial treatment is generally with high-dose intravenous acyclovir, which is the most widely studied and used drug for treating eczema herpeticum¹¹. Valacyclovir and famciclovir are also very effective with better oral bioavailability and a more convenient dosing schedule for patients. The antibiotic therapy is tailored to the organism found on culture, and this is most commonly the *Staphylococcus* species. When a bacterial infection is not present, the patients should be given a topical antibiotic cream like silver sulfadiazine for prevention¹¹. Patients with recurrent HSV infections and a chronic skin disease that predisposes them to eczema herpeticum should be offered prophylaxis with either valacyclovir or acyclovir.

Hailey-Hailey disease was first described by the Hailey brothers in 1939¹². It usually appears in the third or fourth decade, although it can occur at any age. It is a chronic autosomal dominant disorder with incomplete penetrance. Approximately two thirds of patients have a family history of this disorder. A history of multiple relapses and remissions is characteristic. It typically begins as a painful

erosive skin rash in a flexural area. It usually involves the genital area, neck, axillae and popliteal fossae and it recurs in the same locations. Patients typically have recurrent vesicles on an erythematous background. The vesicles rupture and leave an eroded base, and then they generally become crusted. Secondary bacterial infection, which is not uncommon, can give rise to an unpleasant smell. White bands on the fingernails and pits in the palms can also occur^{13,14}. Heat, sweating and friction often exacerbate the disease, and most patients have worse symptoms during the summer months¹⁴.

The responsible defect has been identified in the gene named ATP2C1 on the 57 chromosome 3q21-24, and the gene encodes the human secretory pathway Ca^{2+} -ATPase (hSPCA1) localized in the Golgi apparatus¹⁵. It controls the Ca^{2+} stored in the Golgi bodies. More than 82 different ATP2C1 mutations have currently been described¹⁶. The defect that is responsible has been identified on a gene called *ATP2C1* and the gene is found on chromosome 3q21-24. This gene codes for the protein SPCA1 (Secretory Pathway Calcium/manganese-ATPase), which is a calcium and manganese pump. Ca^{2+} is needed for the assembly of functional adherens junctions and desmosomes. The keratinocytes stick together via desmosomes and it seems that the desmosomes do not assemble properly if there is insufficient calcium. The epidermal Ca^{2+} gradient in the skin is therefore attenuated in the patients with Hailey-Hailey disease. The total Ca^{2+} concentrations were reported to be substantially decreased in the superficial layers of the epidermis, whereas the basal layer of the epidermis and the dermis had unchanged Ca^{2+} concentrations¹⁶. This results in a mechanical defect in the tonofilament-desmosome complex or intercellular substance, leading to the cleavage of the epidermal cells, that is, epidermal acantholysis¹⁶. The disease persists when acantholysis is coupled with repeated minor shearing stress. Viral infections have been implicated in the exacerbation of lesions^{4,14}. It is well known that direct virus transmission by contact with infected persons may evoke eczema herpeticum. These facts suggest that the fragility of the epidermal cells, which results from eczema-like epidermal lesions, makes it easy for herpes simplex virus to infect and proliferate there. Interestingly, the typical lesions of eczema herpeticum in our case occurred in an exposed area like the chin. The location of the eczema herpeticum in our case suggests that the skin involvement was the result of direct inoculation of the herpes simplex virus. Herpes simplex virus infection may be from autoinoculation or from an infected contact¹¹.

The characteristic pathologic finding of Hailey-Hailey disease is suprabasal acantholysis¹⁷. Severe acantholysis is

seen in some lesions, and this finding is diagnostic in the proper clinical setting. Histologically, Hailey-Hailey disease has a characteristic 'dilapidated brick wall appearance'. The pathology in some biopsies may only consist of a suprabasal slit with minimal acantholysis, and such a biopsy may be indistinguishable from that seen in pemphigus vulgaris. Yet the clinical presentation is distinctive. Some cases of Grover's disease (transient or not-so-transient acantholytic dermatosis) may share pathologic features with Hailey-Hailey disease, although dyskeratosis is more commonly seen in Grover's disease.

A variety of therapeutic modalities have been recommended for the treatment of Hailey-Hailey disease. Unfortunately there is no cure for Hailey-Hailey disease. The current therapeutic strategies attempt to suppress Hailey-Hailey outbreaks and allow the patient to live comfortably with this condition. The therapeutic options include antibiotics, corticosteroids¹⁴, systemic and topical cyclosporine¹⁸, oral retinoid and the topical vitamin D analogue¹⁹ and surgical methods such as excision and grafting²⁰ and CO₂ lasers.

To the best of our knowledge, this is the first case report from Korea in which we have described the coexistence of eczema herpeticum and Hailey-Hailey disease.

REFERENCES

1. Yang JS, Kim KM, Lee GJ, Kim IH, Oh CH. Eczema herpeticum in Darier's disease. *Ann Dermatol* 1998;10:32-34.
2. Lee D, Kang SH, Kim JY, Kang MS, Cho SH, Park SW. A case of Darier's disease complicated by eczema herpeticum. *Korean J Dermatol* 2004;42:90-92.
3. Han JH, Choi CJ, Ihm CW. Pemphigus foliaceus complicating eczema herpeticum. *Korean J Dermatol* 1994;32:94-98.
4. Zaim MT, Bickers DR. Herpes simplex associated with Hailey-Hailey disease. *J Am Acad Dermatol* 1987;17:701-702.
5. Flint ID, Spencer DM, Wilkin JK. Eczema herpeticum in association with familial benign chronic pemphigus. *J Am Acad Dermatol* 1993;28:257-259.
6. Schirren H, Schirren CG, Schlupen EM, Volkenandt M, Kind P. Exacerbation of Hailey-Hailey disease by infection with herpes simplex virus. Detection with polymerase chain reaction. *Hautarzt* 1995;46:494-497.
7. Otsuka F, Niimura M, Harada S, Ishibashi Y, Shishiba T. Generalized herpes simplex complicating Hailey-Hailey's disease. *J Dermatol* 1981;8:63-68.
8. Wheeler CE Jr, Abele DC. Eczema herpeticum, primary and recurrent. *Arch Dermatol* 1966;93:162-173.
9. Nishimura M, Maekawa M, Hino Y, Mihara K, Kohda H. Kaposi's varicelliform eruption. Development in a patient with a healing second-degree burn. *Arch Dermatol* 1984;120:799-800.
10. Wollenberg A, Zoch C, Wetzel S, Plewig G, Przybilla B. Predisposing factors and clinical features of eczema herpeticum: a retrospective analysis of 100 cases. *J Am Acad Dermatol* 2003;49:198-205.
11. Mackley CL, Adams DR, Anderson B, Miller JJ. Eczema herpeticum: a dermatologic emergency. *Dermatol Nurs* 2002;14:307-310, 323.
12. Hailey H, Hailey H. Familial benign chronic pemphigus. *Arch Dermatol Syphilol* 1939;39:679-685.
13. Jung MJ, Lee SJ, Cho YW, Han JY, Song KY. Hailey-Hailey disease with a family history and unique nail lesions. *Ann Dermatol* 1999;11:271-275.
14. Burge SM. Hailey-Hailey disease: the clinical features, response to treatment and prognosis. *Br J Dermatol* 1992;126:275-282.
15. Persic-Vojinovic S, Milavec-Puretic V, Dobric I, Rados J, Spoljar S. Disseminated Hailey-Hailey disease treated with topical tacrolimus and oral erythromycin: case report and review of the literature. *Acta Dermatovenerol Croat* 2006;14:253-257.
16. Missiaen L, Raeymaekers L, Dode L, Vanoevelen J, Van Baelen K, Parys JB, et al. SPCA1 pumps and Hailey-Hailey disease. *Biochem Biophys Res Commun* 2004;322:1204-1213.
17. Wilgram GF, Caulfield JB, Lever WF. An electron-microscopic study of acantholysis and dyskeratosis in Hailey's disease. *J Invest Dermatol* 1962;39:373-381.
18. Kim BJ, Seo SJ, Kim MN, Song KY. A case of Hailey-Hailey disease improved with oral cyclosporine. *Korean J Dermatol* 2002;40:1281-1283.
19. Aoki T, Hashimoto H, Koseki S, Hozumi Y, Kondo S. 1alpha,24-dihydroxyvitamin D₃ (tacalcitol) is effective against Hailey-Hailey disease both in vivo and in vitro. *Br J Dermatol* 1998;139:897-901.
20. Oh YS, Lee SY, Song HJ, Kye YC, Kim SN. A case of early onset Hailey-Hailey disease treated with surgical operation. *Ann Dermatol* 1994;6:86-89.