Hailey-Hailey Disease with a Family History and Unique Nail Lesions

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Hailey-Hailey disease(benign familial chronic pemphigus) is a rare autosomal dominant disorder characterized by blisters at sites of friction such as the neck, axillae and groin which are caused by suprabasal epidermal acantholysis.

We report two cases of Hailey-Hailey disease in the one family. One of the two cases has asymptomatic multiple longitudinal white bands in the fingernails associated with typical skin lesions. The nail lesions have not been described until reported by Burge in 1992 and it may be a characteristic finding in Hailey-Hailey disease.

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Key Words : Family history, Hailey-hailey disease, Unique nail lesions.

Hailey-Hailey disease(HHD) is a rare autosomal dominant disorder with a family history in two-thirds of the cases[1]. The disease was first described by the brothers Hailey in 1939[2], and characterized by recurrent blistering lesions with marked predilection for the intertriginous areas. In 1992, Burge[3] reported asymptomatic longitudinal white bands in the fingernails of his patients. We report 2 cases of HHD with a family history and multiple longitudinal white bands in the fingernails of one case.

CASE REPORTS

Case 1.

A 65-year-old woman had had erythematous patches with erosions for the past 40 years. In her pedigree, her grandfather, father, three sons, sister and sister's son were also affected(Fig.1). Laboratory findings including CBC, U/A, LFT, serology and chest roentgenogram were within normal limits. The KOH mount and fungus culture results were negative. On physical examination, there were vesicles on an erythematous base and brownish papules covered with crusts on the belt area and inguinal area(Fig.2), and there were well demarcated eroded patches in the axillary area(Fig. 3). The biopsy specimen taken from the inguinal area revealed hyperplasia, focal parakeratosis, suprabasilar cleft, villi projecting into the cavity and acantholysis of dilapidated brick wall appearance in the epidermis and mild chronic inflammatory cell infiltrations in the dermis(Fig. 4). Under higher magnification, there were partial losses of intercellular cohesion of acantholytic cells. On electron microscopy, acantholysis might be caused by desmosome loss of keratinocytes but basal cells were still adhered to the basement membrane with hemidesmosome, and there were microvilli on the cell membrane(Fig. 5).

Case 2.

A 41-year-old man, the eldest son of case 1, was presented with brownish papules and plaques since 1 year ago. In the laboratory findings, there

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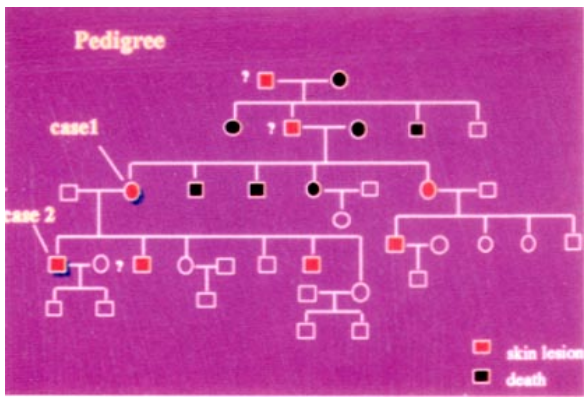

Fig. 1. In pedigree, case 1, her grandfather, father and sons(including case 2) were affected. Except for "?" marked patients, all patients were examined by the author.

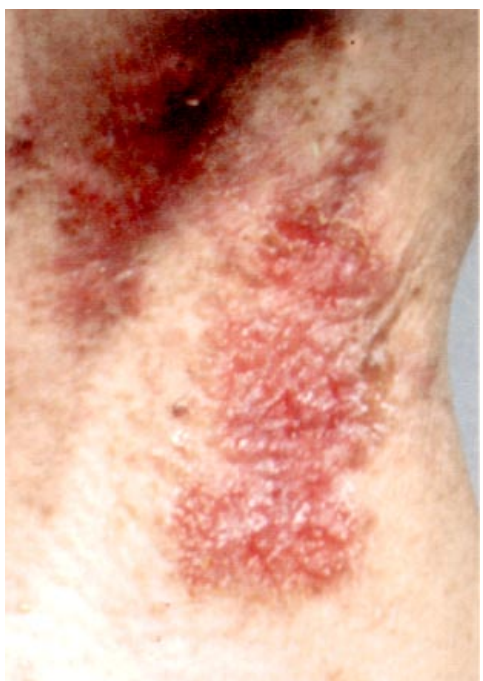

Fig. 3. There are well demarcated eroded patches in the axillary area in case 1.

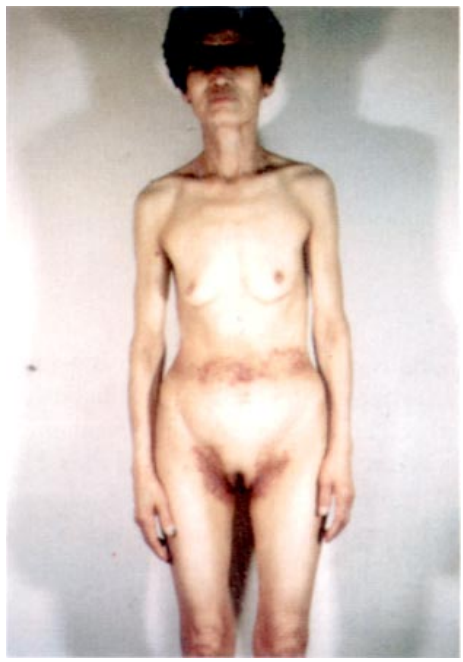

Fig. 2. Brownish papules covered with crusts on the belt area and inguinal area in case 1.

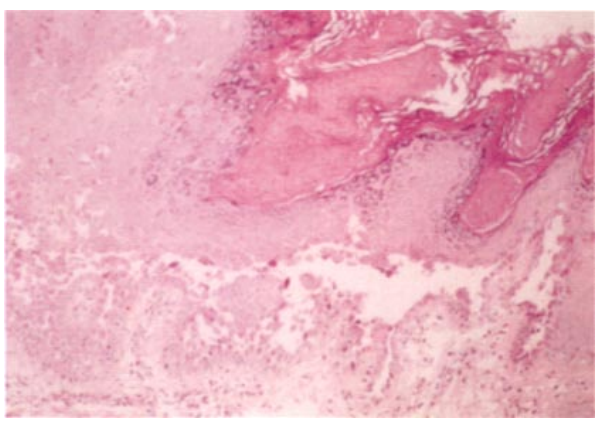

Fig. 4. A specimen taken from the inguinal area of case 1 reveals hyperplasia, focal parakeratosis, suprabasal cleft, villi and dilapidated brick wall appearance in the epidermis(H&E, ×200).

were increased GOT and GPT values, fatty liver findings in an abdominal ultrasonogram were reported, and KOH mount, fungus culture and other laboratory findings were either negative or within normal limits. Clinically, there were multiple hyperkeratotic brownish or erythematous papules and vesicles on an erythematous base in both axilla and groin(Fig. 6), and multiple longitudinal white bands in his fingernails(Fig. 7). We performed a biopsy of the hyperkeratotic papules on the groin. Microscopically, focal hyperkeratosis, dyskeratotic cells similar to corps ronds in the granular layer and acantholysis of dilapidated brick wall appearance in the detached epidermis were presented(Fig. 8).

So, we diagnosed these cases as Hailey-Hailey disease with familial tendency. We treated the cases with topical steroids and antibiotics. After treatment, most of the skin lesions improved with partial hyperpigmentation.

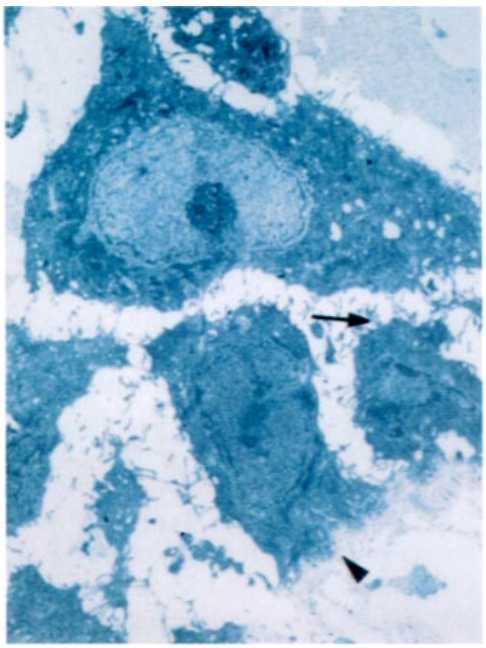

Fig. 5. Electromicroscopically, there are microvilli on the cell membrane(arrow) and loss of desmosome, but basal cells are attached to basement membrane(arrow head) in case 1.

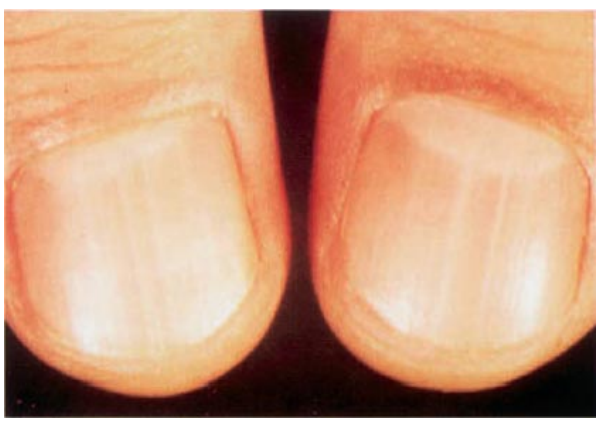

Fig. 7. Multiple longitudinal white bands in the fingernails of case 2.

DISCUSSION

In 1939, Hailey and Hailey[2] described 4 patients and named the condition "benign familial chronic pemphigus". The disease generally presents between the second and fourth decades[3]. Clinically the disease is characterized by a usually localized, recurrent eruption of small vesicles on an erythematous base. Sites of predilection include the sides and back of the neck, groins, perineum and axillae[3]. In

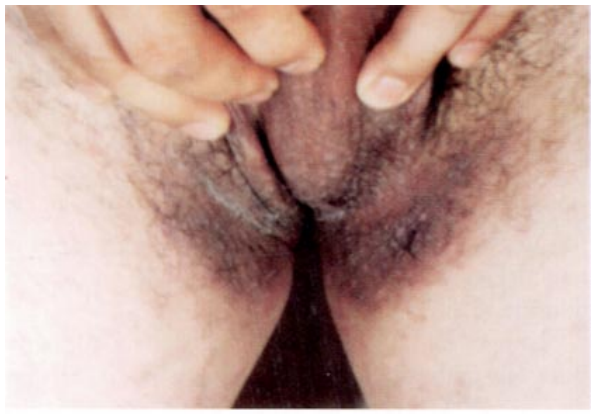

Fig. 6. Multiple hyperkeratotic brownish or erythematous papules and vesicles in both groin of case 2.

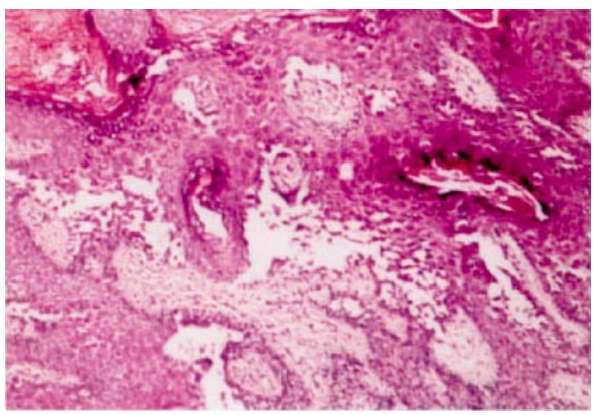

Fig. 8. Microscopically, a specimen of case 2 shows focal hyperkeratosis, dyskeratotic cells similar to corps ronds in the granular layer and acantholysis of dilapidated brick wall appearance in the detached epidermis (H&E, ×200).

the fingernails, asymptomatic longitudinal white bands were first described by Burge in 1992[3], and he reported that the nail lesions presented in 71% of patients examined and were a helpful physical sign[3]. Unlike Darier's disease, the nails in HHD were not fragile or notched and there were no red lines[3]. Morales et al[4]. have proposed that in genetically predisposed persons with HHD, stimulation of the skin by trauma, bacterial or fungal infection, and dermatoses may bring about the overt lesions seen in this disease. Friction, heat or sweating exacerbated the disease and symptoms were worse in the summer than the winter[3]. In genetic studies, Peluso et al[5]. reported a confirmation of the mutant gene to chromosome 3q and further studies proposed several mutant sites on chromosome 3q. In

our cases, case 1 showed erythematous patches with erosions in the intertriginous areas. Case 2 revealed hyperkeratotic papules as well as erythematous patches and asymptomatic longitudinal white bands in his fingernails. Their skin lesions were aggravated by heat, sweating and stress. In this family, the grandfather, father, case 1, three sons(including case 2), sister and sister's son were affected(Fig.1). This pedigree shows autosomal dominant inheritance pattern.

Pathogenesis of HHD is uncertain. But many different pathophysiologic mechanisms have been discussed. A defect of synthesis of intercellular substances6 as well as an epidermal cell dissociating factor[7] have been postulated. However, recent ultrastructural and immunohistochemical investigations provide strong evidence that acantholysis is due to disruption of desmosomes either as a consequence of dysfunction of desmosomal proteins[8] or activation of plasminogen[9]. Metze et al[10]. have suggested that incomplete acantholysis in HHD may be due to a cohesive function of the adherens junction-actin system succeeding the dissolution of desmosomes.

In the histopathologic finding, lesions show suprabasal separations and villi which protrude upward into the bulla. Acantholysis affects large portions of the epidermis but leads to incomplete separation because of a few intact intercellular bridges. That is a typical appearance of a dilapidated brick wall. Some of the acantholytic cells have a homogenized cytoplasm, suggesting premature partial keratinization resembling the grains of Darier's disease. Occasionally, a few corps ronds are present in the granular layer[11]. By electron microscopy, lesions of HHD show bizarre microvillar change, highly electron dense and abnormally thickened bundles of tonofilaments in a whorled or unwhorled configuration in juxtanuclear or perinuclear position, and reduced number of desmosomes6. Basal cells often demonstrate reduced cell adhesions on their lateral and superior surfaces but retained normal attachment to the basement membrane by hemidemosomes.

In the differential diagnosis, impetigo contagiosum show Gram-positive cocci in the bulla cavity, pemphigus vegetans shows reactive patterns in the immunofluorescence technique, and transient acantholytic dermatosis may exhibit small foci of intraepidermal acantholysis, but these are only a few rete wide. The clinical features of HHD may overlap with those of Darier's disease, but Darier's disease generally has an earlier onset, the progress of the disease is unaffected by topical steroids, the lesions are not induced by minor trauma, and its major clinical findings are keratotic papules on the trunk and palmar pits or keratotic palmar papules3. Histopathologically, in Darier's disease the suprabasal separations are usually smaller, acantholysis is less pronounced, being limited to the lower epidermis, and dyskeratosis is much more evident[11]. In our cases, case 1 had a typical incomplete acantholysis with villi. Electromicroscopically there were microvilli on the cell membrane and loss of desmosome as well as a separation of epidermal cells but basal cells were attached to the basement membrane with hemidesmosomes. Case 2 showed hyperkeratotic papules on inguinal areas similar to Darier's disease but histopathologically demonstrated not only some dyskeratotic cells but also acantholysis of dilapidated brick wall appearance.

The treatment includes systemic administration of antibiotics, steroid, dapsone[12] and retinoid[13,14], topical application of antibiotics and steroid15 and surgical methods such as excision and grafting16, dermabrasion17 and CO2 laser vaporization18. We have treated the patients with topical steroids and antibiotics and followed them up. The course of the disease has chronically repeated remissions and relapses, but fortunately many patients improve as they get older[3].

We introduce 2 cases of HHD with a family history and case 2 shows multiple longitudinal white bands in the nails which are a helpful physical sign in HHD and not yet documented in Korea until now.

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