Case Report

Dystrophic epidermolysis bullosa presenting as scarring skin eruptions and nail dystrophy

失養症性大疱性表皮鬆解表現為疤痕性皮損及指趾甲失養症

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A 57-year-old Chinese gentleman presented with pruritic skin eruptions located mainly over the shins since childhood. Scratching resulted in skin blister and finally scarring. He also had nail dystrophy over the fingers and toes since childhood. Incisional skin biopsy for histology and electron microscopy was compatible with the diagnosis of dystrophic epidermolysis bullosa. His mother had "prurigo nodularis" and nail dystrophy, but she was not available for examination as she lived abroad. His siblings, children and father were free of skin diseases. He was given symptomatic treatment with topical steroid, eurax cream and oral antihistamine. Antibiotics and local antiseptic solution were used to control skin infections. His pruritic symptom was under control, although the skin scarring and nail dystrophy remained the same.

Keywords: Chinese, dystrophic epidermolysis bullosa

Introduction

Epidermolysis bullosa (EB) is a group of heterogeneous diseases characterised by development of blister after minor mechanical trauma. There are three types of inherited EB and they differ from one another by the level of skin cleavage. ¹ Epidermolysis bullosa simplex has skin cleavage located at basal keratinocytes, whereas, site of skin cleavage of junctional epidermolysis...
Dystrophic epidermolysis bullosa is localised at the intra-lamina lucida region. Dystrophic epidermolysis bullosa (DEB) is characterised by blister developing in the sublamina densa region. The latter entity, although rare, has been previously reported in Hong Kong Chinese. We described another case of dystrophic epidermolysis bullosa in a 57-year-old Chinese.

Case report

A 57-year-old Chinese gentleman, with a known history of asthma, presented to our skin clinic in 1986 with pruritic skin eruptions. These were localised mainly over the shins. The elbows and trunk were involved to a lesser extent. The skin eruption had been developing since childhood. Scratching of the skin was followed by the formation of skin blister and, finally, scarring. He noticed that his shins were easily traumatised with minor injury. At the same time, nail dystrophy developed insidiously over his fingers and toes since childhood. There was no mucosal involvement. He had multiple dental caries with teeth extraction in the recent few years. Systemic symptoms such as weight loss, dysphagia and constipation were absent. Skin biopsy had been performed in Taiwan in the year 1970 but the patient was not sure of the result. He was given five to six courses of steroid injection in Taiwan with only temporary symptomatic relief. His parent's marriage was nonconsanguinous. He had five siblings and two children, all of them did not have any similar skin problem or nail dystrophy as recalled by the patient. His mother had a history of prurigo nodularis and dystrophic toenails. She had never received any skin biopsy but unfortunately, she could not come for examination as she resided in the United States.

Physical examination of the index patient revealed scarring and erosions located symmetrically over both shins and calves (Figure 1). There were hypopigmented scars over the upper back, abdominal walls and both elbows. Apart from androgenetic alopecia, there was no other hair abnormality. There was neither any milium nor blister at the time of examination. His fingernails and toenails were rudimentary and dystrophic (Figures 2 & 3). Taking into account of the timing of onset and the clinical features as summarised above, the most likely clinical diagnosis was DEB. The other clinical differential diagnoses might include lichen planus, prurigo nodularis and epidermolysis bullosa acquisita. Investigations including complete blood picture, liver and renal function tests were normal. Incisional biopsy of skin lesion over the lower limb showed re-epithelialised, pauci-inflammatory subepidermal blister with underlying dermal scarring (Figure 4). Direct immunofluorescence study was negative. However, localisation of lamina dense in blister by histochemical and immunohistochemical methods yield equivocal results. Fortunately, electron microscopy confirmed the presence of lamina densa in roof of blister in many areas. The anchoring fibrils, however, were morphologically unremarkable. The overall features were compatible with DEB. He was given topical steroid, eurax cream and oral antihistamine for symptomatic relief. Topical chlortetracycline...
ointment and potassium permanganate solution were given for eroded areas. The pruritic symptom remained under control with treatment, although he occasionally developed blisters and erosions over his shins on minor trauma.

**Discussion**

DEB is a heterogeneous collection of inherited mechanobullous disorder with characteristic trauma-induced blisters, associated with milia, scarring and nail dystrophy. Ultrastructurally, there is a sublamina densa level of blister formation and quantitative or qualitative changes in anchoring fibrils at the dermo-epidermal junction. DEB can be subdivided into commonly observed types and rare types. Commonly observed subtypes included dominant DEB, recessive DEB-Hallopeau-Siemens (HS) and recessive DEB-non HS. The rare types were clinically striking and included dominant DEB-preternial, DEB-transient bullous dermolysis of the newborn, dominant DEB-pruriginosa, recessive DEB-inversa, recessive DEB-centripetalis and DEB, autosomal dominant/recessive heterozygote. Our patients have pruritic eruptions involving mostly the shins. Features compatible with either pretibial EB or DEB-pruriginosa are present. Pretibial EB features recurrent blistering with scarring and milia formation predominantly in the pretibial area and variable nail dystrophy. In pretibial EB, involvement of other areas of body, besides pretibial region, is not unusual. Moreover pruitus is common and prurigo-like lesions can be present. EB pruriginosa was first described by
Dystrophic epidermolysis bullosa

McGrath et al in 1994. It is characterised clinically by pruritus, lichenified or prurigo-nodularis like lesions, violaceous linear scarring, occasional trauma-induced blistering, milia and nail dystrophy. The lesions are mostly located over the shins, but are also prominent on forearms and sometimes on the trunk. Thus, there are substantial similarities between pretibial EB and EB pruriginosa.

Pathologically, DEB presents as subepidermal blister/cleft and the basal cells appear intact. There is a moderate to heavy upper to mid-dermal interstitial and perivascular lymphohistiocytic infiltrate. Fibrosis may be present in papillary dermis. Milia may also be seen. There are several non-molecular histological diagnostic methods for EB, namely electron microscopy, immunofluorescence antigen mapping and EB-specific antibodies. Electron microscopy demonstrates the level of skin cleavage directly and in DEB, it is in the sublamina densa. Immunofluorescence antigen mapping infers the level of cleavage from fluorescence staining of epidermal antigens and in DEB, bullous pemphigoid antigen-1, laminin-5 and type IV collagen are all in the roof of blister. LH 7:2 antibody binds to the N-terminal of type VII collagen. In recessive DEB, there is reduced or absent staining by this antibody whereas in dominant DEB, the staining is normal.

DEB results from mutations in the COL7A1 gene, which is located on chromosome 3p21 and encodes type VII collagen. Type VII collagen is the major constituent of anchoring fibrils in the dermoepidermal junction and is synthesised primarily by keratinocytes and less by dermal fibroblasts. Three polypeptides, proa1(VII) chains, fold into typical triple helix. Type VII collagen has a central triple helix domain consisting of Gly-X-Y repeats, flanked by two noncollagen domains. Most dominant DEB patients have mutations resulting in glycine substitution in the Gly-X-Y repeats. Although a full-length polypeptide is produced, the triple helix is not as stable as the normal type VII collagen. This leads to clinical phenotype of dominant DEB. In contrast, the more severe clinical phenotype of recessive DEB results from mutations leading to truncated type VII collagen polypeptide. Pedigree analysis is important in deducing the possible mode of inheritance and genetic counselling. But in the absence of an informative pedigree, detection of collagen mutation, if available, can be useful. This has been applied to detect a de novo mutation in dominant DEB and a recessive splice site mutation in pretibial EB. Moreover, the dominant clinical phenotype of DEB can be manifested as familial nail dystrophy, with or without skin eruptions. It is therefore important to examine skin as well as nails in relatives of DEB patients.

Treatment of DEB includes avoidance of trauma, use of nonadherent dressings for wound and treatment of wound infection if present. Skin grafts, either allografts or autografts, have also been tried but there is no proper randomised trial on this treatment modality. Gene therapy is only in the early stage of development. Gene corrected fibroblasts, from patients with recessive DEB, have shown to be able to restore type VII collagen expression in skin equivalent culture and in animal models. It is hoped that gene therapy can provide a final solution for DEB, especially for the recessive form, which is essentially a genetic disease.

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