

Pretibial Epidermolysis Bullosa

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CASE SUMMARY

History

A 12-year-old boy presented with a history of blistering due to trauma on both shins since birth. They healed with scarring and milia formation. The lesions mainly affected the shins and some occasionally appeared on the waist. They were mildly pruritic and were worse in the summer as well as being precipitated by trauma. There was also toenail dystrophy but his hair and teeth were normal. He had been treated with a combination of topical steroid (clobetasol propionate) and antifungal cream (clotrimazole) leading to some improvement. There was no mucosal involvement. There was no significant medical history and he was not on any regular medication. His mother had similar nail changes but no skin lesions. His maternal uncle also had similar lesions on the shins but none of his immediate family was affected.



Figure 1: Blisters, adjacent scarring, milia and lichenoid papules on the shins

Physical examination

On examination, there were isolated blisters on both shins with adjacent scarring, milia and lichenoid papules (Figure 1). There was nail dystrophy on both feet (Figure 2). His mucosa and dentition were normal. General examination was normal. The differential diagnosis included pretibial epidermolysis bullosa, bullous lichen planus, bullous lupus erythematosus and bullous pemphigoid.

Investigations

Blood tests for complete blood picture, renal and liver functions, anti-nuclear factor and anti-skin antibodies were normal. Two skin biopsies were performed. The first skin biopsy showed subepidermal blistering with necrosis of the keratinocytes, hyperkeratosis and a dense perivascular lymphoid infiltrate extending to the deep dermis. There were also many interstitial and perivascular eosinophils. Electron microscopy showed a normal number of anchoring fibrils and the level of split occurred at the lamina lucida.

A second skin biopsy showed re-epithelialized subepidermal blister containing fibrinous material. Electron microscopy showed the split at the sublamina densa (Figure 3). There was an absence or reduced number of anchoring fibrils in the blistering area. When present, the anchoring fibrils were short and attenuated (Figure 4). The hemidesmosomes and anchoring fibrils



Figure 2: Toe nail dystrophy

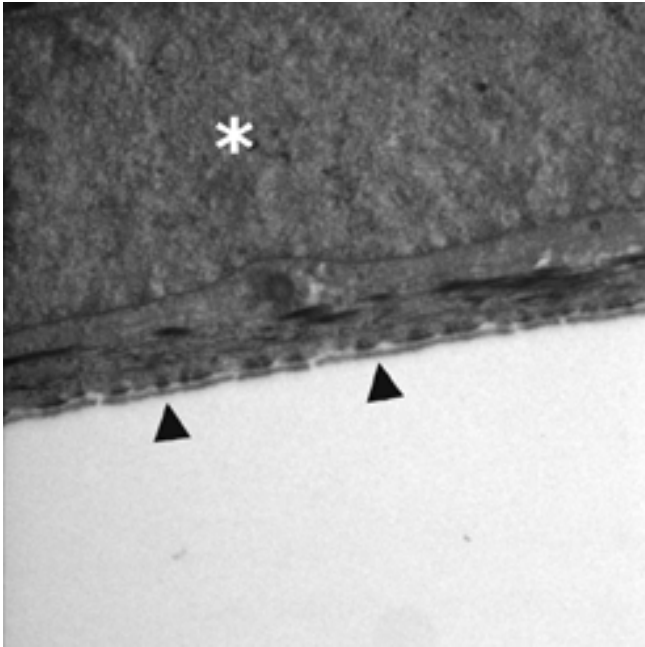


Figure 3: Pretibial EB. Ultrastructurally dermolytic separation immediately beneath the basal lamina (arrowheads) is evident. The basal cells (*) are intact. (By courtesy of Dr. K.C. Lee, Department of Pathology, PMH)

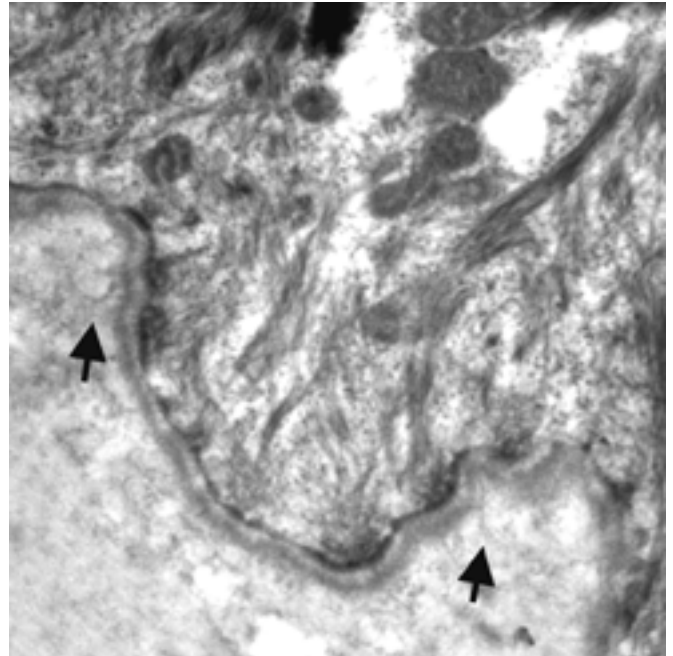


Figure 4: Pretibial EB. Ultrastructural examination of the basement membrane zone shows the anchoring fibrils are either completely absent or are small and attenuated (arrows). (By courtesy of Dr. K.C. Lee, Department of Pathology, PMH)

were normal in the non-blistering areas. The histological findings were compatible with EPIDERMOLYSIS BULLOSA. Clinically, as the lesions were located mainly on the shins, the diagnosis was consistent with **Pretibial Epidermolysis Bullosa**.

Progress

The patient was treated with topical steroids and potassium permanganate soaks. The blisters resolved and the pruritus was relieved by topical steroids. The patient was advised to avoid trauma.

REVIEW ON PRETIBIAL EPIDERMOLYSIS BULLOSA

Definition and epidemiology

Pretibial epidermolysis bullosa (PEB) is a rare form of dominant dystrophic epidermolysis bullosa (DDEB) and was first described by Kuske in 1946.¹ He reported erosions and scarring affecting the shins in three patients from three generations in the same family.

The incidence of PEB is unknown. Apart from isolated cases, the inheritance pattern is mainly autosomal dominant. It may be more common than suspected as it can be misdiagnosed as other inflammatory diseases. Type VII collagen is a major component of the anchoring fibrils. Its molecules form dimeric structures that assemble into anchoring fibrils. Its gene has been mapped to chromosome 3p21. Mutations in the type VII collagen gene (COL7A1) lead to abnormal anchoring fibrils and increased skin fragility. Various mutations in this gene have been reported with PEB, for example, glycine substitution in COL7A1 was reported in a Taiwanese family.² Another mutation is the recessively inherited 14 bp deletion at the 115 exon-intron boundary. This results in the elimination of 29 amino-acids from the pro- α 1 (VII) polypeptide chain,³ and interferes with the conversion of procollagen VII into collagen VII. This mutation has been designated 33563del14.

Clinical features

Dominant dystrophic epidermolysis bullosa (DDEB) can be divided into the Cockayne-Touraine and

Pasini variants. The pattern of inheritance is autosomal dominant in both types. In the Cockayne-Touraine type, the onset is in infancy and the blisters are usually localized to the extremities that heal with milia formation. There are also nail dystrophy and occasional hypertrophic scar formation. In the Pasini variant, the onset is in infancy with more extensive blistering that heals with atrophic scars and milia. This variant is characterized by albopapuloid lesions on the trunk that occur independently of the blisters. Recessive DEB is divided into localized and generalized severe forms and the onset is also in infancy or early childhood.

PEB is a localized form of DDEB and the age of onset is delayed, occurring between three and 24 years of age. The disease is milder and characterized by trauma-related blistering localized to the shins. They heal with scarring and milia formation. In some cases, albopapuloid lesions are present and the clinical picture may overlap with other forms of DDEB. As a result of this, there has been controversy as to whether PEB is a separate entity. Intra-familial variability may lead to difficulties in diagnosis and confusion with other inflammatory dermatoses such as eczema and lichen planus. In addition, the presence of blisters is often

overshadowed by the lichenoid papules, which leads to misdiagnosis.

In Hong Kong, three patients with PEB had been reported previously (Table 1).⁴ In all cases, the patients had been misdiagnosed as suffering from eczema, lichen planus or prurigo before the correct diagnosis was made. The relatively late onset together with dermal infiltrate seen on histological examination can lead to misdiagnosis and under-reporting of the condition.

The mode of inheritance in these cases was unknown. In the present case, the presence of similar nail changes in the mother, and similar skin and nail changes in the maternal uncle suggest the presence of an affected gene. Although the inheritance pattern is autosomal dominant in most cases, PEB has been reported as a sporadic case in a series in Taiwan.⁵ In some of the cases, features overlapping with the Cockayne-Touraine and Pasini variants (lesions not confined to the tibia, albopapuloid lesions, hypertrophic scars) were present. The lesions were worse in summer and in hot, humid environments. The clinical course was progressive in most cases, especially after puberty.

Table 1. Reported cases of PEB in Hong Kong⁴

| Patient | History | Skin biopsy |
|-------------------------|--|---|
| Patient 1 M/17 years | Trauma-induced blisters, lichenoid papules, vesicles, toe nail dystrophy and milia on the shins and elbows since childhood | Dense upper dermal infiltrate with dermal fibrosis |
| | Brother has a similar condition but sister not affected | Immunofluorescence negative |
| | Previous diagnoses: eczema, tinea, lichen planus | Electron microscopy (EM): reduced anchoring fibrils in peri-lesional skin and sublamina densa blister |
| Patient 2 M/12 years | Brother of patient 1 | Histology as above |
| | Lichenoid papules, milia, vesicles on the shins Toe nail dystrophy | EM showed absent anchoring fibrils in the peri-lesional skin and a sublamina blister |
| Patient 3 F/22 years | Not related to the above cases | Histology and EM as above |
| | Pruritus, vesicles on the legs since four years old | |
| | Lichenoid papules, pigmentary changes on the extensor surfaces of the legs | |
| | Teeth, hair and nail normal | |
| | Previous diagnoses: eczema, prurigo | |

Histology

In light microscopy, a subepidermal blister and a moderately dense lymphocytic infiltrate may be present. This may lead to misdiagnosis as other inflammatory dermatoses. Electron microscopy shows rudimentary or absent anchoring fibrils in lesional and non-lesional skin. The level of blister cleavage is beneath the lamina densa. The abnormalities of the anchoring fibrils do not distinguish PEB from other types of DEB. The hemidesmosomes are often normal.

Differential diagnosis

The differential diagnosis includes lichen planus, prurigo nodularis, blistering disorders such as bullous lupus erythematosus and bullous pemphigoid.

Treatment

Treatment consists mainly of avoidance of trauma and wound care. Secondary infection can be treated with antibiotics while topical steroids are effective in relieving pruritus. Due to the localized nature of this disease, patients are less severely affected than other types of dystrophic EB. In terms of genetic counseling, the parents can be informed that the inheritance is autosomal dominant, but specific data from gene studies is not available for this condition in Hong Kong.

Learning points:

Pretibial epidermolysis bullosa may be more common than reported and may mimic inflammatory skin disorders such as prurigo nodularis and lichen planus. Increased awareness of this condition will enable earlier diagnosis and appropriate management.

References

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