Case report

DOMINANT DYSTROPHIC EPIDERMOLYSIS BULLOSA, LOCALIZED (MINIMUS) TYPE. REPORT OF A KINSHIP

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ABSTRACT

A kinship of patients with dominant dystrophic epidermolysis bullosa characterized by blistering, which subsided in the majority of cases in the first months of life, is reported. The lesions healed without scarring but in two instances deformity of the nails, developed later on. There was no involvement of the mucous membranes and no congenital skin defect. Micromorphology disclosed a sub-basal lamina separation. Ultrastructural findings are presented. The relevant literature is reviewed.

KEY WORDS

epidermolysis bullosa, Bart's syndrome, transient bullous dermolysis of the newborn

INTRODUCTION

Recently in U.S.A. a subcommittee established by the National Epidermolysis Bullosa Registry issued criteria for the practical diagnosis and classification of patients with inherited epidermolysis bullosa. They separated common and well-established forms of epidermolysis bullosa from rarer or less well-established ones. They suggested that most patients could be best classified as having one of three major presentations (generalized, localized and inverse) of three major subsets (simplex, junctional and dystrophic), of Herlitz versus non Herlitz and dominant versus recessive transmitted forms (1).

We describe a family with epidermolysis bullosa characterized by following features: 1) blistering which subsided within six months of life in the majority of patients: the lesions healed entirely without scarring leaving only transitory "milia" which cleared in a few months or years; 2) deformity of the nails; 3) no involvement of the mucous membranes; 4) absence of congenital skin defects; 5) sub-basal lamina separation was revealed by electron microscopic analysis of the lesions.

These findings are consistent with the diagnosis of dominant dystrophic epidermolysis bullosa, localized (minimus) type (1, 2).

CASE REPORTS

A female infant (Case No. 1) was born at full term by vaginal delivery to a 28-years-old primigravida woman. It

weighed 3500 g and had Apgar scores of 9 and 10 at 1 and 5 minutes respectively. The infant's parents were in good health, but questioning revealed a history of bullous disorders in the mother's family. At the time of birth, the newborn had no skin lesions, but at the age of six months bullae appeared on the lower and upper extremities (Fig. 1.). Periblister skin appeared normal. The bullae healed entirely without scarring, within some months , and only a few "milia" remained (Fig. 2.). No lesions of the nails or mucous membranes were found. Now at the age of 40 months the child tolerates normal activities without renewed blistering. She is without scars and only a few minimal "milia" are present.

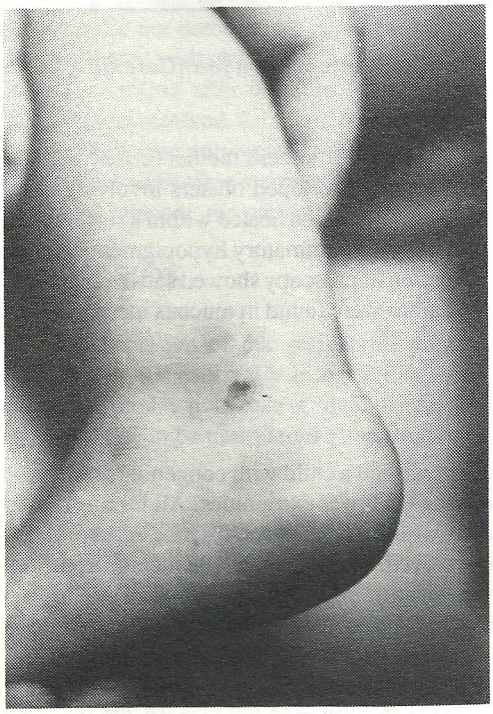

Fig. 1. Small blister on the left foot at 7 months of age (Case No. 1).

The results of the following laboratory studies were within normal limits or negative: complete blood count, differential, uric acid, albumin, total protein, magnesium, calcium, cultures of skin for bacteria, urinalysis, liver function tests. Biopsy specimens were taken from fresh bullae and included adjacent normal skin. Hematoxylin-eosin revealed a subepidermal blister with minimal inflammation. The ultrastructural examination confirmed that the blister was intradermic; the site of cleavage was at the dermo-epidermal junction, just below the basal lamina (Fig. 3 a.). At higher magnification it was clearly seen the integrity of the hemidesmosomes, lamina lucida and lamina densa; the most consistent submicroscopic

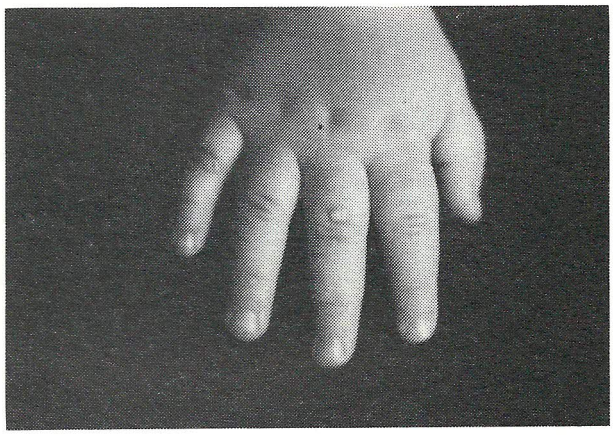

Fig. 2. Minimal "milia" are seen in healed areas of the right hand at 11 months of age (Case No. 1).

defect was the absence or the hypoplasia of anchoring fibrils (Fig. 3b.). Occasionally a variable amount of the dermal material remained attached to the undersurface of the basal lamina, but otherwise separation left the basal lamina essentially bare.

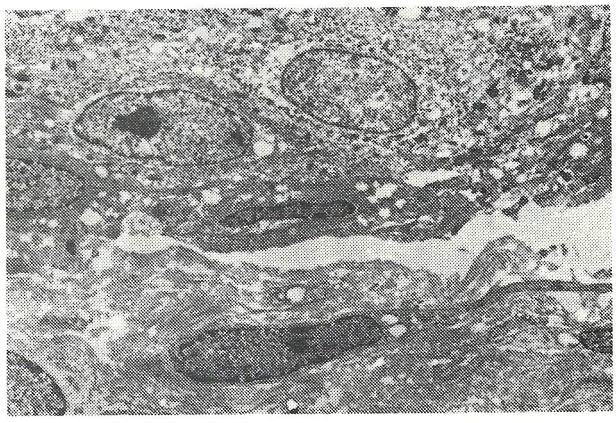

Fig. 3a. Ultrastructural findings demonstrate that the separation occurred in the level just below the basal lamina. Dermal fibroblasts showed activation features because the rough endoplasmic reticulum system is hyperplastic. There is reduction of anchoring fibrils (Electron microscopy: x 5600).

Dermal fibroblasts appeared numerous and showed activation features because their rough endoplasmic reticulum system was hyperplastic.

Additional information from the parents disclosed that the child's mother (Case No. 2), the mother's mother (Case No. 3) and several members of the mother's family showed bullae

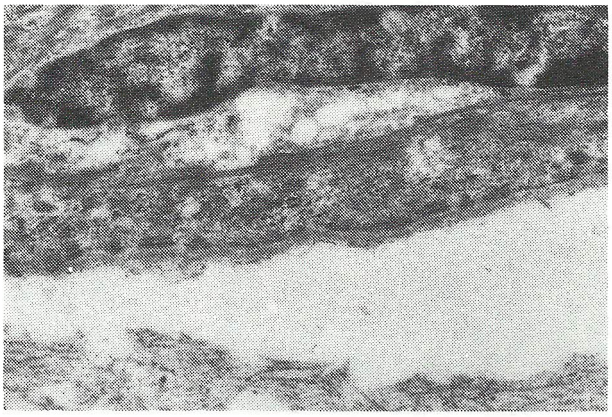

Fig. 3b. Higher magnification shows the integrity of the hemidesmosomes and the basal lamina. The reduction of anchoring fibrils is clearly seen (Electron microscopy: x 32000).

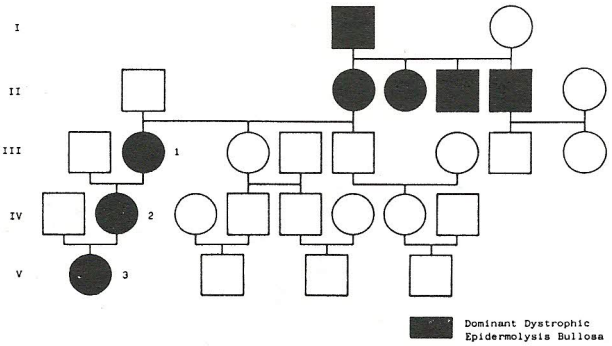

Fig. 4. Family pedigree (Patient Nos. 1,2 and 3 in pedigree correspond to cases Nos. 3, 2,1, respectively, in text).

induced by minimal trauma on the lower and upper extremities at the age of a few months. A pedigree of this family is shown in Fig. 4., only three members were directly questioned and examined.

Information regarding other members or those members who were deceased was obtained from the personal physicians of the affected members or other family members over the last five generations.

All lesions healed in a few months without scarring. Moreover the child's mother (Case No. 2) showed a nail deformity on both hands and feet which began several years after birth. Similar lesions were expressed in the child's grandmother (Case No.3) (Fig. 5.). No information on this defect could be obtained regarding other relatives.

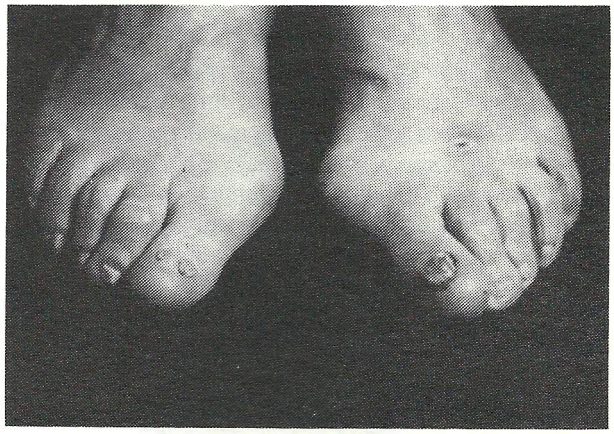

Fig. 5. Dystrophic nails are seen on feet (Case No. 3).

At the age of 49 years the mother's mother (Case No. 3), at the time of menopause, developed blisters involving arms and lower part of the legs which healed within a few months leaving only slight postinflammatory hypopigmentation. In this case also, electron microscopy showed sub-basal lamina separation. No lesions were found in mucous membranes in any cases.

DISCUSSION

In 1966 Bart described a child with congenital absence of the skin, involving the lower extremities. All lesions healed without scarring within a few years. Absence or deformities of nails were observed. The kinship of 103 members showed 26 affected persons (3).

The original family described by Bart, which presented as heterogeneous entity, had a fully penetrant autosomal trait. Two families with many similarities to those of the kinship described by Bart were reported by Joensen (4). In 1986 Butler first reported microscopic, ultrastructural and immunofluorescent mapping studies of an individual of an affected group with "Bart's syndrome" and considered this syndrome as a mild form of dominant dystrophic epidermolysis bullosa associated with congenital absence of skin, in which marked improvement or abatement of the blistering may occur after puberty (5). Despite improvements in diagnosis by immunofluorescence mapping and monoclonal antibodies, transmission electron microscopy is still the most appropriate procedure for practical diagnosis (EB simplex, junctional, dystrophic) of these diseases.

Another constant feature, common to familial cases, is the transiency of blister formation however the family reported by Bart (3) included an affected member who continued to develop lesions up to 42 years of age. This suggests that

"Bart's syndrome" consists of a wide range of lesions differing in extent, intensity and time of appearence. However the healing of the erosions, without sequelae, but sometimes transitory "milia" and no recurrence of sub-basal bullae since the age of a few years, is one of the major criteria for establishing this diagnosis.

Skin biopsy provides a picture of separation of the epidermis from the dermis above the basal layer. However in several cases histological study and electron microscopy were not performed, making comparison with other cases in the literature difficult.

In 1985 and 1989 Hashimoto (6,7) reported three isolated cases of a neonatal blistering disease that healed spontaneously within a few months. Two patients had normal skin at birth but multiple blisters subsequently developed, the third at birth had large areas of denudation on both hands, and within 2 days blisters developed on the legs and in the axillae. The mucous membranes were affected in only one case, and there was no nail dystrophy. The bullae were also sub-basal.

The most consistent ultrastructural defect in our patients was the absence or the hypoplasia of anchoring fibrils as reported by other authors (6,7) and dermal fibroblasts showing activation features as evidenced by rough endoplasmic reticulum system. We were not able to see the stellate inclusions in dilated rough endoplasmic reticulum in the keratinocytes of the lower epidermis, described by Hashimoto et al. (7)

Our cases are characterized by sub-basal transient blistering and a dominant autosomal inheritance with variable penetrance. In contrast to familial cases of "Bart's syndrome" which sometimes present congenital absence of skin, our cases do not show these features. Moreover, they have many similarities with Hashimoto's cases but differ in two important respects: the mode of inheritance and the development of blistering several months after birth.

This report gives rise to three hypotheses: 1) that familial cases of transient bullous dermolysis of the newborn (or rather within six months of life) may exist. This family shows many similarities to those of the kinship described by Bart (3) and the sporadic case of transient dermolysis of the newborn described by Hashimoto (6,7), but some features suggest that this is either 2) a variant of Bart's syndrome (without the absence of skin at birth, but not excluding its manifestations in the following) or 3) a minimal form of the rare dominant dystrophic epidermolysis bullosa as recently reported by Fine et aI (1).

Reappearence of blistering in the mother's mother (Case No. 3) at the age of menopause may suggest a hormonal implication.

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