Epidermolysis bullosa of the Weber-Cockayne type with macular amyloidosis[1]

Gary R. Kantor, M.D.
James M. Kasick, M.D.
Wilma F. Bergfeld, M.D.
James T. McMahon, Ph.D.
John A. Krebs, M.D.[2]

Various forms of epidermolysis bullosa have been rarely associated with amyloidosis. A case is presented of a child with epidermolysis bullosa of the Weber-Cockayne type and macular amyloidosis. A possible mechanism for both diseases may involve basal cell lysosomal activation.

Index terms: Amyloidosis • Epidermolysis bullosa

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Epidermolysis bullosa of the Weber-Cockayne type is a dominantly inherited nonscarring mechanobullous disease characterized by bullae localized to the hands and feet. Ultrastructurally, epidermolysis of the basal cell occurs, resulting in blister formation between the basal cell nucleus and the dermal-epidermal junction.[1] The mechanism of these cytolytic changes is unknown. We report a patient with epidermolysis bullosa of Weber-Cockayne associated with macular amyloidosis.

Case report

A 5-year-old-white girl presented in August 1983 with a four-year history of blisters on her feet at sites of friction. Also, an asymptomatic telangiectatic patch had appeared in infancy on the hands and feet and gradually extended to involve the arms and legs during the past four years. The patient's general health was excellent with no recent illnesses or infections. Family history included an affected brother, age 6, with bullous eruptions on the hands and feet that ultramicroscopically showed intracellular edema between the basal layer and the dermal-epidermal junction consistent with epidermolysis bullosa of Weber-Cockayne. Amyloid deposits were not found in the dermis or around blood vessels. The patient's father reported a history of bullae on the hands and feet as a child.

Physical examination revealed bullae on the plantar aspect of the toes and heels. No milia, nail dystrophy, or oral lesions were present. A reticulated telangiectatic patch was present on the dorsal aspect of the hands and feet (*Fig. 1*) and extended proximally to the arms and thighs.

Biopsy of the bullae was not performed. Histologic evaluation of a skin biopsy specimen of the telangiectatic patch on the right thigh showed capillary ectasia. Toluidine blue staining of a plastic-imbedded section of a skin biopsy spec-

[1] Departments of Dermatology (G.R.K., J.M.K., W.F.B., J.A.K.) and Pathology (W.F.B., J.T.M.), The Cleveland Clinic Foundation. Submitted for publication March 1985; accepted April 1985. ht
[2] Currently in private practice, Sandusky, OH. Former fellow, Department of Dermatology, Cleveland Clinic.

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A, B

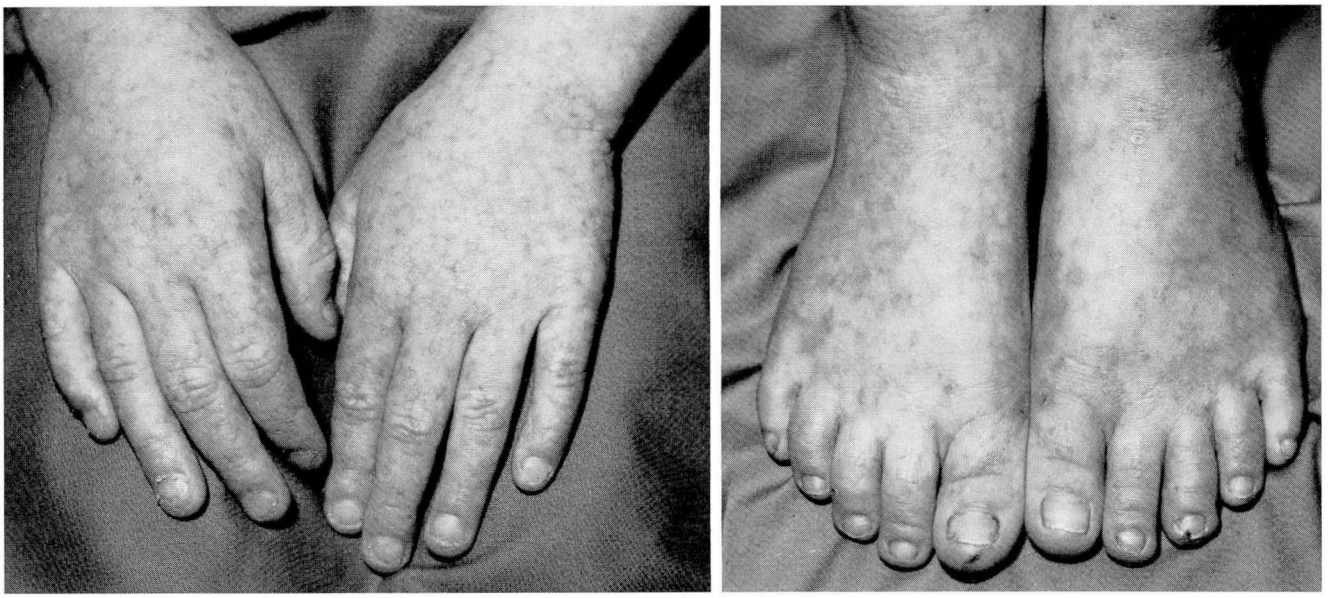

Fig. 1. Reticulated telangiectatic patch on dorsal aspect of hands (**A**) and feet (**B**). Note erosions on distal right great toe and left third toe.

Table. Classification of epidermolysis bullosa (EB)

Form	Location of Blister	Mode of Inheritance	Clinical Characteristics
1. EB simplex	Intraepidermal	Autosomal dominant	Generalized nonscarring bullae
2. EB of Weber-Cockayne	Intraepidermal	Autosomal dominant	Bullae localized to hands and feet
3. EB letalis	Dermoepidermal junction	Autosomal recessive	Multiple nonscarring denuded lesions present at birth; frequently fatal
4. Generalized atrophic benign EB	Dermoepidermal junction	Autosomal recessive	Generalized bullae associated with alopecia, nail changes, and oral lesions; good prognosis
5. EB dystrophica—dominant	Upper dermis	Autosomal dominant	Scarring with or without preceding bullae at birth or early infancy; nails thickened or absent and oral lesions uncommon
6. EB dystrophica—recessive	Upper dermis	Autosomal recessive	Localized or generalized forms; ulcers, scars, mucous membrane and esophageal involvement, nail loss, syndactyly and contractures; sometimes fatal
7. EB acquisita	Upper dermis	None	Scarring blisters at trauma sites in adults; nail dystrophy common

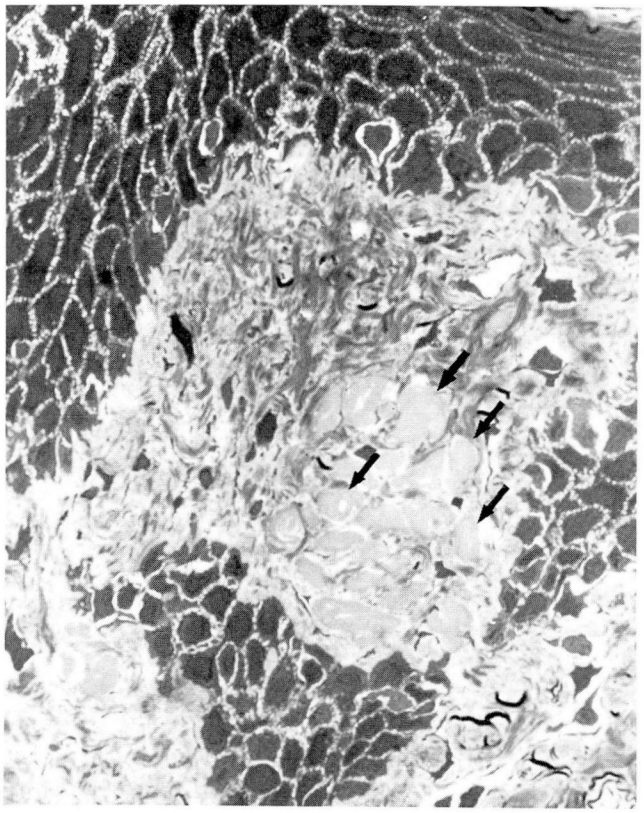

Fig. 2. Plastic-imbedded section of a skin biopsy specimen showing clusters of gray bodies (arrows) in papillary dermis (Toluidine blue, original magnification ×480). Immunostaining for kappa and lambda chains was negative. Congo red, crystal violet, and thioflavin T stains did not satisfactorily demonstrate the bodies.

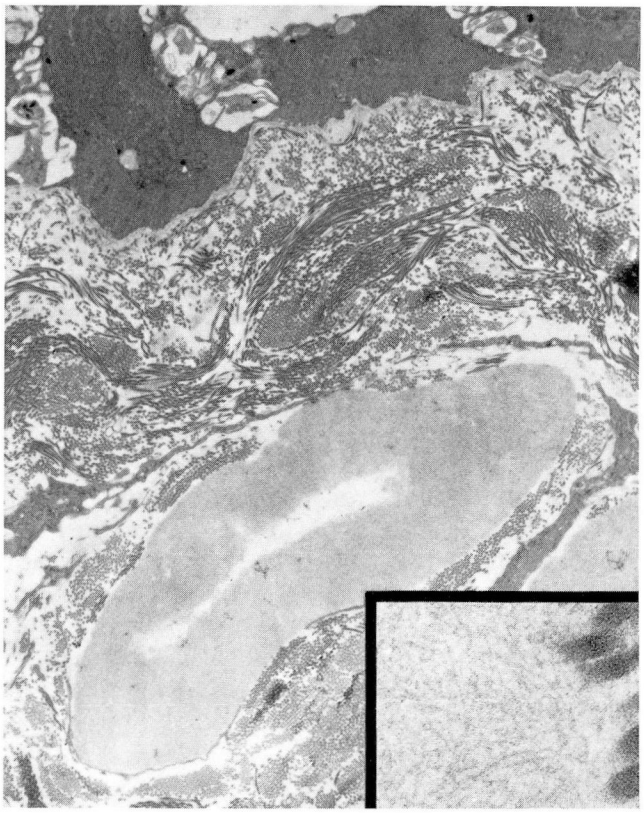

Fig. 3. Electron micrograph of upper dermis and overlying epidermis. Within the papillary dermis is a nodular electron-lucent zone, which, on high magnification (inset), contains fine nonbranching fibrillar structures measuring 10–16 nm.

imen demonstrated distinct blue-gray bodies subjacent to the dermal-epidermal junction (*Fig. 2*). Electron microscopic examination revealed that these bodies had the characteristic fibrillar pattern of amyloid (*Fig. 3*). The vascular structures were spared of amyloid deposition.

Laboratory evaluation included normal or negative test values for complete blood count, serum protein electrophoresis, serum porphyrins, antinuclear factor, anti-deoxyribonuclease, anti-extractable nuclear antigen, SS-A, SS-B, urinalysis, urine porphyrins, and urine protein electrophoresis.

Discussion

Kyle[2] classified amyloidosis into five types: primary amyloidosis with no evidence of preceding or coexisting disease; amyloidosis with multiple myeloma; secondary amyloidosis coexisting with chronic diseases such as rheumatoid arthritis or infection; localized amyloidosis that involves a single organ; and familial amyloidosis. Localized amyloidosis of the skin appears in three forms: nodular or tumefactive; lichenoid; and macular. The nodular form may occur as a sign of systemic amyloidosis whereas lichenoid and macular amyloidosis only involve the skin.

Macular amyloidosis classically presents as hyperpigmented pruritic patches typically on the back and proximal extremities. Absent epidermal hyperplasia helps differentiate macular amyloidosis from lichen amyloidosus.

Epidermolysis bullosa (EB) has been classified into seven types based on the ultrastructural site of blister formation, mode of inheritance, and clinical characteristics (*Table*). In all forms, blisters form as a result of minor trauma.[3] EB of the Weber-Cockayne type has bullae limited to the hands and feet with disease exacerbation in the summer. Bullae heal without scarring and the mucous membranes and nails are unaffected.

Ridley and Levy[4] cited four cases of EB associated with secondary systemic amyloidosis: EB acquisita, EB dystrophica, and two cases of EB vegetans. In addition, they described a case of EB letalis associated with primary amyloidosis. EB acquisita may also be associated with visceral amyloidosis.[5,6] To our knowledge, our patient is the first reported case of EB of Weber-Cockayne associated with macular amyloidosis.

We classify our patient's amyloidosis as the macular form because of the lack of epidermal changes or documented systemic involvement. We speculate that amyloid deposition in the papillary dermis promoted the development of telangiectasia of the skin. It is doubtful that our patient had bullous amyloidosis[7] mimicking EB of Weber-Cockayne, considering the family history, histologic and ultrastructural confirmation in a sibling, and lack of bullae on the skin except for the feet. In addition, although macular amyloid deposits can be associated with inflammatory conditions such as dyskeratosis congenita,[8] no preceding inflammation was reported by our patient.

The amyloid in macular amyloidosis originates from degenerating epidermal cells that are discharged into the dermis.[9] It is believed that cellular lysosomes digest tonofilaments to produce the amyloid material.[9] The mechanism of epidermolysis in EB of Weber-Cockayne is unknown but may involve cellular lysosomes. Therefore, a mechanism for both amyloid deposition and epidermolysis may involve lysosomal activation. Further ultrastructural evaluation of a larger series of patients with EB of Weber-Cockayne is needed to determine whether macular amyloidosis is an associated abnormality or a factor in bullae formation at friction sites.

Department of Dermatology
Cleveland Clinic Foundation
9500 Euclid Avenue
Cleveland, OH 44106

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