A Case of Diffuse Biphasic Cutaneous Amyloidosis

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We described a case of diffuse biphasic cutaneous amyloidosis, a unique form of localized cutaneous amyloidosis. A 41-year-old man has gradually developed a lichenoid papular and a grouped spotted pigmented macular eruption on the trunk and upper extremities over the past 15 years. Histopathologic examination revealed that amyloid deposits were present in the papillary dermis. It was confirmed by Congo red staining, immunohistochemistry and electron microscopy. There was no evidence of systemic amyloidosis.
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Key Words : Diffuse biphasic cutaneous amyloidosis

The clinical patterns of primary localized cutaneous amyloidosis (PLCA) are currently classified as macular, papular and nodular[1]. The lesions of macular amyloidosis (MA) are moderately pruritic, symmetrically distributed, brown, rippled macules over the upper back and the interscapular areas[2]. Lichen amyloidosis (LA) is characterized by the appearance of paroxysmally itchy lichenoid papules, typically on the shins, with intense pruritus[3]. Both forms can be seen in the same patient and even the conversion of MA to the lichenoid form has been observed[4-6]. We herein described a case of this biphasic variant of diffuse cutaneous amyloidosis with unusual manifestations.

CASE REPORT

A 41-year-old man presented with a diffuse maculopapular eruption involving the trunk and upper extremities. He complained of little pruritus. The first lesions had appeared on the trunk 15 years ago and subsequently had gradually spread to the upper extremities. There was no family history of any similar condition. Examination revealed symmetrically distributed, diffuse, hyperkeratotic, lichenoid papular and grouped, spotted, pigmented macular lesions located predominantly over the upper back and upper arms (Fig. 1). The pattern varied from arcuate and whorled over the back to linear arrangement over the upper arms.

Multiple skin biopsies were obtained from the macular and the papular lesions. Sections from pigmented macules revealed foci of faintly eosinophilic material in the dermal papillae. The epidermis showed focal hyperkeratosis, hypergranulosis, flattening of the rete ridges and increased melanin granules in the stratum corneum. Pigmentary incontinence was also present. The lichenoid lesions also revealed nodular deposits of pale pinkish material containing clefts and melanophages in the papillary dermis, and marked hyperkeratosis, hypergranulosis and acanthosis in the epidermis (Fig. 2). None of the sections showed evidence of basal cell degeneration and there were no amyloid deposits around the blood vessels, the appendages or the dermal collagen.

Congo red stain with a polarizing microscope demonstrated apple-green birefringence of amorphous deposits in the dermal papillae from the specimen of macular lesion in the upper back (Fig. 3). They were weakly PAS-positive but negative with elastic staining from the specimen of macular lesion in the upper back. Immunohistochemical staining was positive for cytokeratin (Fig. 4), but neg-

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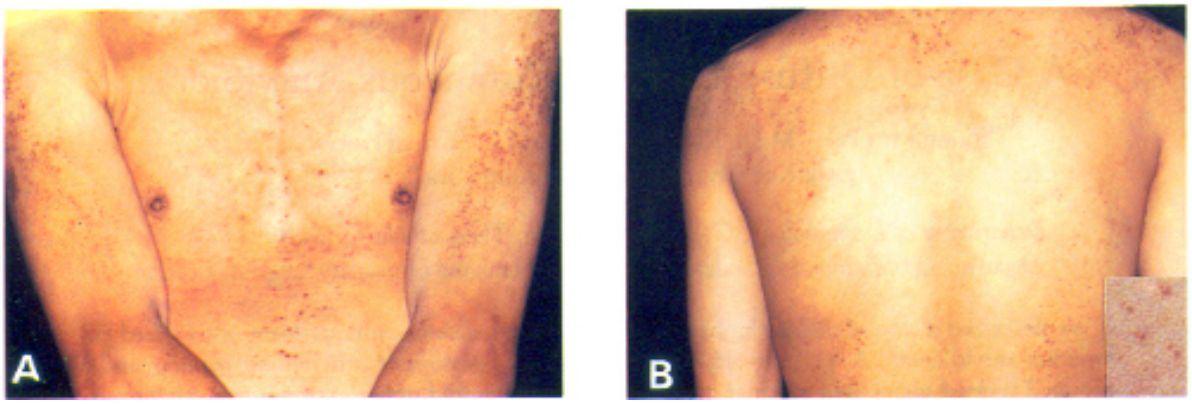

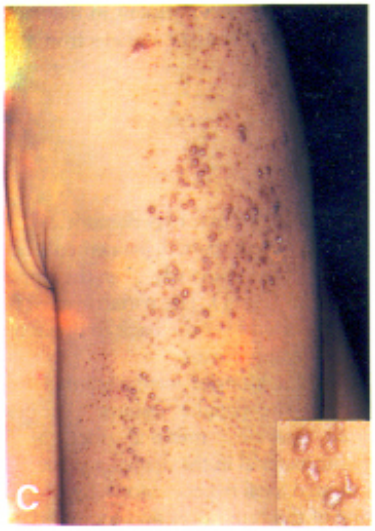

Fig. 1. A. Symmetrically distributed, diffuse, hyperkeratotic, lichenoid papular and grouped, spotted macular lesions over the chest, abdomen and both upper arms B. Diffuse, pigmented macular lesions with arcuate and whorling appearance on the back (inset : close up view of macular lesions). C. Linear hyperkeratotic, lichenoid papular and pigmented macular lesions on the left upper arm (inset : close up view of papular lesions).

ative for kappa and lambda chains, laminin, type IV collagen, and amyloid A protein from the specimen of macular lesion in the upper back.

Electron microscopic examination showed nodular deposits of amyloid within the dermal papillae from the specimen of macular lesion in the upper back (Fig. 5). The amyloid deposits consisted of a disordered meshwork of nonbranching fibrils with diameters ranging from 7.5 to 10 nm. The amyloid were found in the extracellular matrix intermixed with varying numbers of collagen fibers

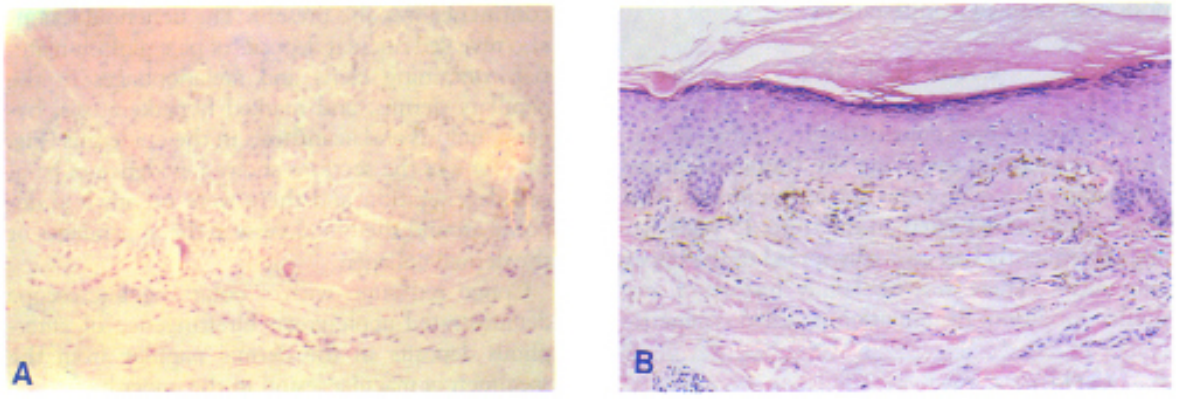

Fig. 2. A. Nodular deposits of pale pinkish material containing clefts in the dermal papillae and marked hyperkeratosis, hypergranulosis, acanthosis, hyperpigmentation of basal layer from the specimen of lichenoid lesion in the left upper arm. B. Faintly eosinophilic amorphous material with clefts and pigmentary incontinece in the dermal papilla and flattening of the rete ridge from the specimen of macular lesion in the upper back (H & E, ×100).

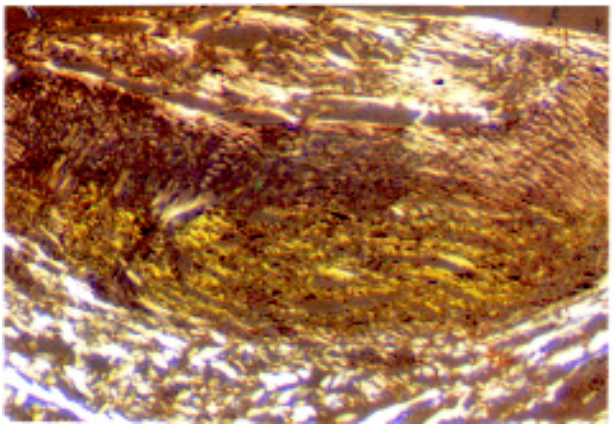

Fig. 3. Apple-green birefringence of amyloid deposits in the dermal papillae from specimen of macular lesion in the upper back (Congo red stain with polarizing microscope, ×100).

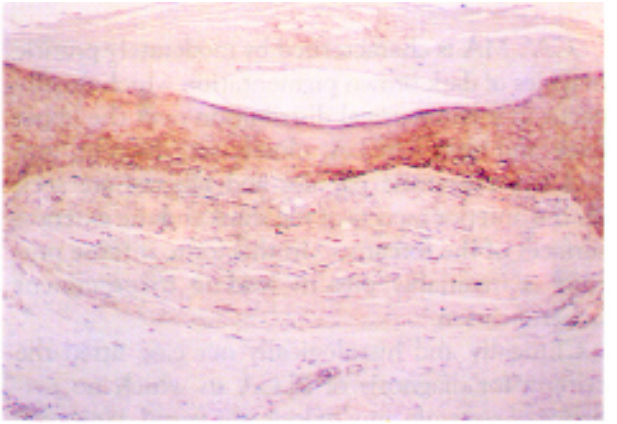

Fig. 4. Micrograph showing positive staining pattern of the amyloid deposits in the dermal papillae by indirect immunohistochemical method using an anti-keratin antibody from the specimen of macular lesion in the upper back (×100).

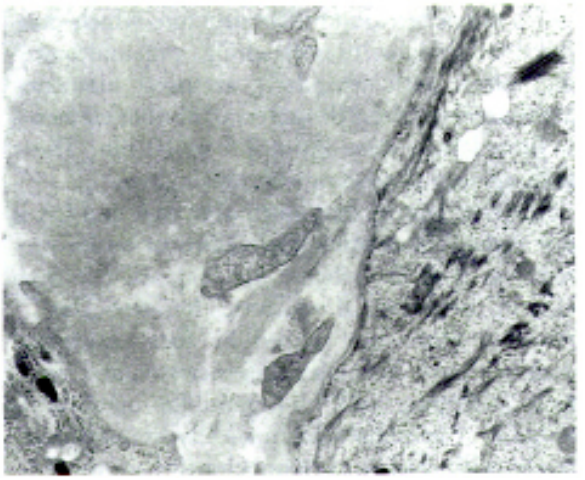

Fig. 5. Randomly arranged amyloid fibrils within the dermal papillae from the specimen of macular lesion in the upper back (E.M. ×10,000).

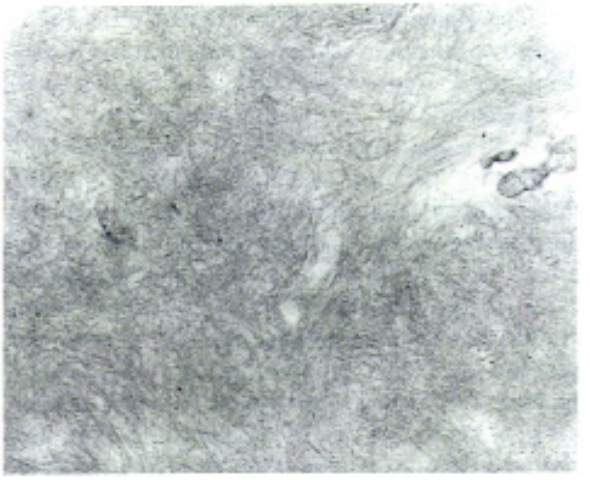

Fig. 6. A meshwork of amyloid fibrils with diameters ranging from 7.5 to 10 nm from the specimen of macular lesion in the upper back (E.M. ×25,000).

from the specimen of macular lesion in the upper back (Fig. 6).

All other investigations (complete blood count, biochemical profiles, plasma protein electrophoresis, serum immunoglobulins, urinalysis and examination of Bence-Jones protein, rheumatoid factor, chest X-ray) were normal or negative.

He was treated with oral (etretinate, 0.5 mg/kg/day) and topical retinoids (0.1% tretinoin cream) for 2 months, but there was no improvement.

DISCUSSION

Amyloidosis has been divided into primary (idiopathic) and secondary amyloidosis, which may be either systemic (visceral) or cutaneous[1]. Amyloid deposits in the skin are seen either in the primary systemic amyloidosis or the benign PLCA which is virtually never associated with systemic diseases[7]. PLCA refers to the clinically significant deposition of amyloid, limited to the skin, unassociated with any underlying dermatologic or systemic disease[1]. LA and MA are two closely related forms of

PLCA[8]. MA is characterized by moderately pruritic macules of dark brown pigmentation which usually occur in a symmetrical distribution over the upper back and arms[2]. In LA, closely-set, discrete, firm and hyperkeratotic papules and plaques are seen on the anterior aspects of the shins and the extensor surfaces of the forearms[3]. In this form, intense pruritus is invariably present leading to prominent lichenification.

Clinically and histologically our case fitted the criteria for diagnosis of PLCA in which no evidence of systemic amyloidosis was found. However, the present case showed unusual manifestations of PLCA. First, this case exhibited the dimorphous appearance (both lichenoid and macular forms) of PLCA. Brownstein et al.[4] proposed the term "biphasic amyloidosis" to this mixed form of PLCA. Second, our patient had grouped spotted macular pigmentation rather than a reticulated, rippled or confluent pattern as a characteristic and diagnostic feature of MA. Third, some macular areas of pigmentation gradually transformed into lichenoid lesions over a number of years. Kibbi et al.[9] proposed a spectrum for PLCA, in which the less itchy classical macular variant occurs at one end and the very pruritic traditional lichen variant at the other. In 42% of patients with MA, intermediate cases having macular lesions with micropapular and/or lichens were identified. The spectral expression of PLCA in the form of MA, LA or biphasic variant seems to depend on many factors, yet to be known[6]. It has been suggested that they can change from one into the other: from MA to LA as a result of chronic irritation of the skin from scratching[6], and from LA to MA under treatment with an intralesional injection of corticosteroids[4]. However, this patient had little pruritus and physical examination revealed no scratch marks or lichenification. He also had no history of medication for skin lesions. Fourth, Our patient showed an unusual localization of lichenoid lesions which appeared diffusely over the entire trunk and upper extremities. Moreover, there was no involvement of lichenoid lesions on the shins as in classic LA. The occurrence of widely disseminated lesions in either LA or MA is rare and diffuse involvement of the skin with both types of lesions in the same patient is even rarer[5].

The diagnosis of PLCA depends on the histochemical, immunohistochemical, or ultrastructural demonstration of amyloid material in a skin[10]. In this case, histopathologic examination showed deposits of eosinophilic material in the dermal papillae. Marked hyperkeratosis, papillomatosis, and epidermal hyperplasia were also noted in the lichenoid lesion. Congo red stain with polarizing microscopy revealed apple-green birefrigence of nodular deposits in the dermal papillae. Unfortunately, methyl violet and Congo red staining may be equivocal and inadequate for detecting small deposits of amyloid; false-positive results occur in colloid millium and lipoid proteinosis[10,11]. False-positive staining with thioflavin T is seen with stromal hyaline deposits, collagen fibers, and colloid bodies in lichen planus[10]. Thus, none of the existing stains are absolutely reliable, and an ultrastructural study may sometimes be necessary. Electron microscopic examination demonstrated that they had a characteristic fibrillar structure which consisted of straight, nonbranching, nonanastomosing, often with irregularly arranged filaments. Measurement of the diameters of fibrillar elements indicated they were about 7.5 to 10 nm. These findings were consistent with amyloidosis.

It is now known that amyloid in MA and LA is not derived from immunoglobulins or serum proteins, as it is in systemic amyloidoses, but from keratin peptides of necrotic keratinocytes[10,11]. Amyloid fibrils are formed by local epidermal damage from tonofilament degeneration and apoptosis (dropping off)[1,10]. Keratinlike material is found in it immunohistochemically, staining positively with EKH4, a monoclonal keratin antibody[1]. In this case, we also immunohistochemically observed a positive staining pattern for cytokeratin at the site of amyloid deposition, although staining was more intense in the epidermis. These findings suggested that the amyloid was of epidermal origin, at least in part.

Treatment of primary localized cutaneous amyloidosis is frequently unsatisfactory. MA and LA unfortunately respond poorly to topical steroids combined with systemic antihistamines to alleviate pruritus[10]. Dermabrasion has been advocated for LA[12]. There have been anecdotal reports of response to topical DMSO therapy in some patients[13,14], but not in others[15]. Etretinate therapy may also be beneficial in a proportion of patients[16,17] but not in all[18]. This patient was treated with oral and topical retinoids for 2 months, but

there was no improvement of the skin lesions.

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