Lichen amyloidosus of Freudenthal.

Case report

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SUMMARY

We present a case of lichen amyloidosus of the legs with clinical features similar to those of lichen simplex chronicus. The nosology, classification of cutaneous amyloidosis and etiology of amyloid formation are discussed.

KEY WORDS

lichen amyloidosus, amyloid, case rereport

Introduction

The term amyloidoses encompasses a broad spectrum of conditions related to disturbances of protein metabolism. Each subset shows distinct features as for etiopathogenesis, clinical presentation and prognosis.

Clinically, amyloidoses are divided into *systemic forms*, where the severe multiorgan impairment frequently leads to a fatal outcome, and *localized forms*, the course is related to the involved sites.

All amyloidoses are characterized by extracellular deposition of an inert substance, showing distinct tinctorial and physicochemical properties due to the particular configuration of its "major" (fibrillary) component. Crystallographic x-ray diffraction and spectrometry disclosed that fibrils are formed by polypeptide chains, characterized by folds arranged perpendicularly to the longitudinal axis of the fibrils in the distinctive cross-β pattern.

All types of amyloidosis are usually unresponsive to therapeutical approach. We herein report a case of cutaneous circumscribed lichenoid amyloidosis doing well under topical steroid treatment. (1)

Case report

A 35-year-old male with a 10-year history of papular lesions was referred to us. The lesions, preceded and accompanied by pruritus, were initially located on the posterior aspect of his right leg and subsequently spread on both the legs.

Physical examination revealed non-confluent papular lesions on the anterior and posterior aspect of both legs. The lesions were roundish, dome-shaped, 3 to 4 mm in diameter, pink to brownish in color, with a

smooth or horny surface. Perilesional skin showed some mild, brownish reticulated hyperpigmentation. (Figure 1)

There were no skin diseases in the family history. Laboratory tests (including electrophoresis and immunoelectrophoresis for Bence Jones proteinuria detection in serum and urine, calcium and creatinine serum level determination, liver function tests, and electrocardiogram) were all within the normal range.

At low magnification (x10), histologic sections stained with hematoxylin-eosin showed parakeratotic hyperkeratosis, acanthosis and papillomatosis, overall reminiscent of chronic lichen simplex. (Figure 2)

Higher magnification (x25), however, disclosed epidermal hyperplasia, prematurely keratinized cells within the spinous layer, and pincer-shaped deformations of interpapillary crests. The latter appeared to wrap up an amorphous, weakly eosinophilic and fissured matrix, deposited in the papillary dermis. (Figure 3)

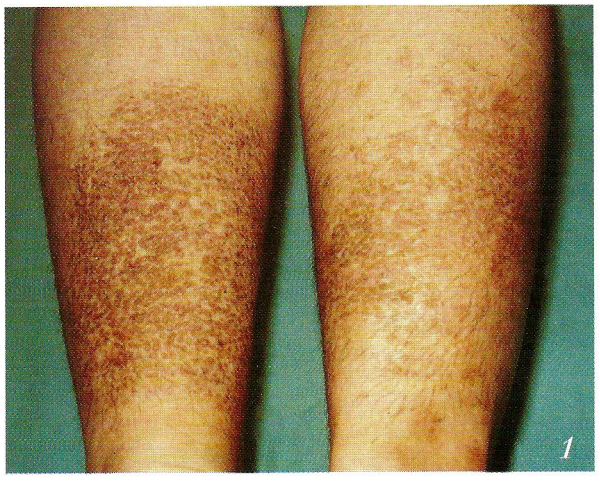


Figure 1. Multiple lichenoid brownish papules on the posterior aspect of the legs with reticulated hyperpigmentation of the perilesional skin.

On the basis of these findings the colloidal or amyloid nature of this material was hypothesized. Confirmatory evidence was ultimately obtained by the following findings: crystal violet metachromasia, congophilia with apple green birefringence under polarized light, and thioflavine T fluorescence. (Figures 4, 5)

On the basis of the above clinical, histological and tinctorial features, the diagnosis of lichen amyloidosus of Freudenthal was made.

A 3-week course of topical steroids under occlusive dressing and oral antihistamines resulted in improvement of symptoms and a decrease in lesion thickness.

Discussion

Cutaneous amyloidoses may be an expression of a systemic disease (in myeloma-associated or secondary forms) or simply a pathology of an isolated organ as in

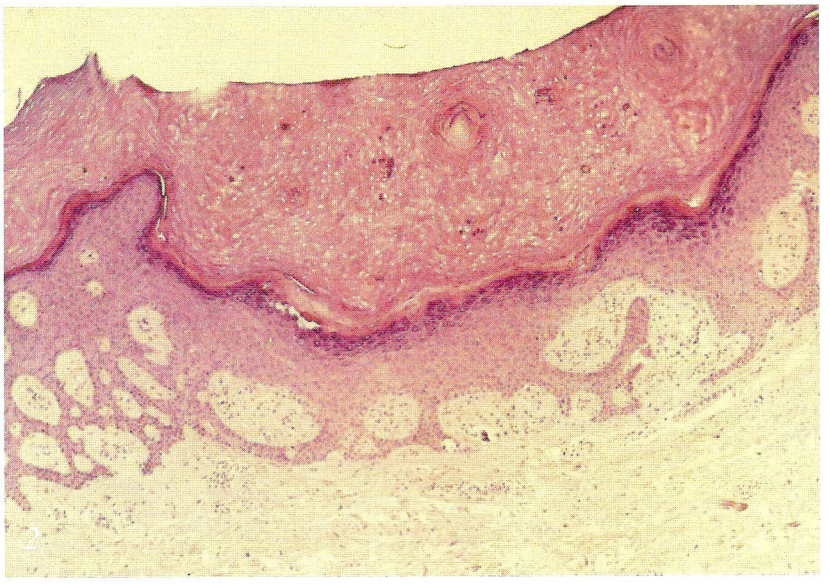
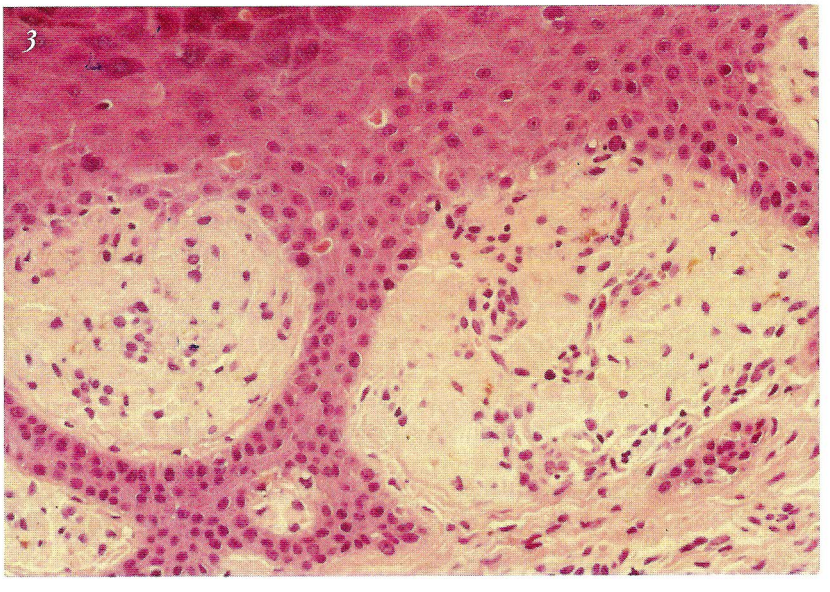


Figure 2. Histopathologic findings of a biopsy specimen, hematoxylin and eosin stain x 10. Hyperkeratosis, acanthosis and papillomatosis of epidermis can be seen, reminiscent of chronic lichen simplex.

Figure 3. Higher magnification (x25) revealed prematurely keratinized cells within the spinous layer, and amorphous and homogeneous eosinophilic deposits in papillary dermis.



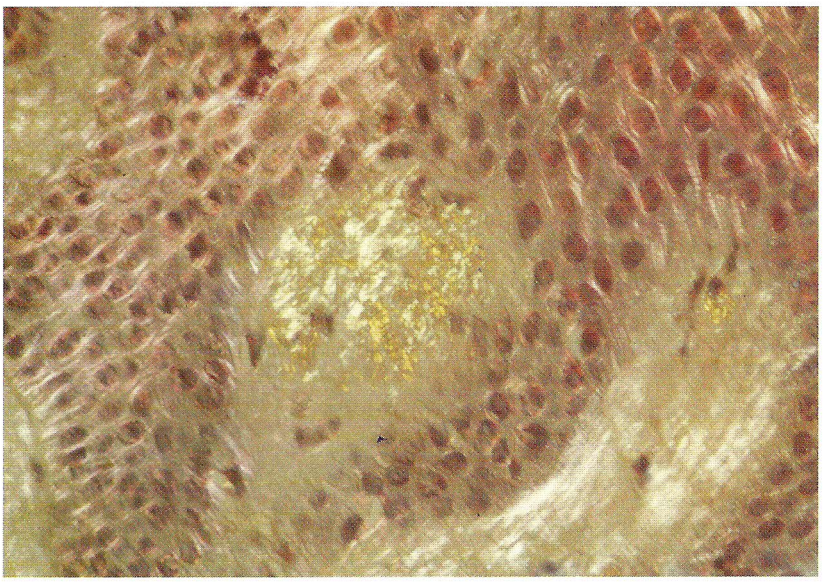


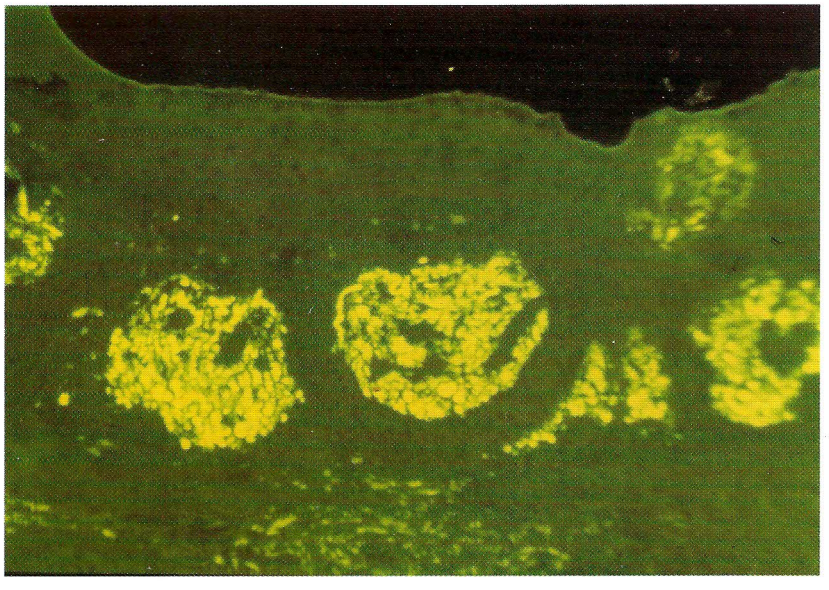
Figure 4. Apple green birefringence on Congo red staining under polarized light.

this case. The latter may occur either as a sporadic or heredofamiliar form, with clinical manifestations limited to the skin, or be related to genodermatoses (e.g. Partington disease) or neurological pathologies. (2-4)

Modern diagnostic methods, using monoclonal antibodies, have identified more than 15 proteins in the fibrillary portion of amyloid.

The most frequently detected in the skin are the amyloid AL (L= light) or immune amyloid, the amyloid AA (A=α1-glicoprotein, produced in the acute phase of the inflammatory reaction), the apoptosis amyloid or amyloid K (K=keratin) and the β-microglobulin (a nonglycosylated polypeptide present on nucleated cells) in haemodialysis-associated amyloidosis. (1)

Figure 5. Fluorescence with thioflavine T demonstrates the presence of amyloid deposits in the upper dermis.



Primary keratogenic amyloidosis (PKA), or Gutmann's circumscribed primary amyloidosis, is an organ-limited subset in which the skin is the exclusive site of involvement. Two forms of PKA may be distinguished: a macular type with reticulated hyperpigmentation or poikiloderma, localized especially on the trunk and less frequently on the limbs, and a lichen type, known also as "lichen amyloidosus of Freudenthal", characterized by pruritic papular, hyperkeratotic lesions, mainly located on the lower limbs. (5) Intermediate clinical forms have also been described, in which both macular and papular lesions occur in the same patient. (6-9)

Electron microscopy has shown that amyloid fibrils are the results of metabolic degeneration of keratinocyte tonofilaments, which develop into the interepidermal filamentous masses (or Civatte's bodies) as an intermediate product. Even though the epidermal origin of this substance has been confirmed, the cause of such degenerative process and the mechanism involved is yet unknown. (10)

The pathogenesis of the clinical lesions is also not perfectly clear; it seems that agents such as UVA radiation, pruritus and scratching, capable of causing focal damage in the epidermal cells, determine the formation of amyloid in the papillary dermis. (11-14)

However, the absence of pruritus in some patients with lichen amyloidosus, cannot explain the lichenified aspect of the skin, normally related to repeated scratching.

On the other hand, the existence of familial cases suggests the importance of genetic factors in the etiology of both macular and lichen amyloidosus. (3) In normal subjects, the presence of apoptotic keratinocytes induces phagocytosis by macrophages and neutrophils, while in patients with lichen or macular amyloidosis, a genetic deficiency of this scavenging mechanism causes an abnormal accumulation of degenerated keratin giving rise to cytoid bodies or amyloid deposits. (10)

Primary cutaneous amyloidosis, to which our case seems to belong, includes forms of amyloidoses related to neoplastic and non-neoplastic skin conditions, such as psoriasis, solar and senile keratoses, (14) Bowen's disease, basal cell carcinoma (15) and adnexal neoplasms.

Numerous other cutaneous pathologies are to be considered in the clinical differential diagnosis of lichen amyloidosus: Darier's disease, Grover's disease, pityri-

asis rubra pilaris and secondary lichenification.

Darier's disease is characterized by follicular papules, mainly located in the seborrhoeic areas of the face and trunk; familial history along with suprabasal acantholysis and dyskeratosis will confirm the diagnosis.

Grover's disease presents red or violet papules, usually isolated and localized on the anterior thoracic region, and histologically characterized by acantholysis. Pityriasis rubra pilaris shows erythematous patches with follicular hyperkeratosis and desquamation at the knees and elbows; the histological picture is overall psoriasiform, but the presence of stratified hyperkeratosis at the infundibulum points to the diagnosis. The hallmark of lichen ruber planus are the typical violet-red polygonal papules and the histopathology including a rich band-like, lymphohystiocytic infiltrate in the papillary dermis.

From the histological point of view amyloid must be differentiated from pseudo milium colloid, which presents the same tinctorial properties (positivity to Congo red and thioflavine T). However, in pseudo milium colloid the direct relationship between the focus of colloid degeneration and the altered dermal elastic fibers is almost constantly obvious. Moreover, this material is separated from an intact epidermis by a thin layer (grenz zone). (17-19)

The treatment of primary localized cutaneous amyloidosis, both in the macular and the papular type, is usually symptomatic and consists of systemic antihistamines and topical application of corticosteroids. (6)

Some authors have proposed dermabrasion (20) as an effective treatment for papular lichen amyloidosus, while other authors have suggested the use of dimethylsulfoxid (DMSO) (21-23) (a solvent normally used to increase transcutaneous absorption of some drugs). The efficacy of systemic etretinate (24) and cyclophosphamide (6) seems to be controversial.

This case seemed worth presenting for its rarity and to stress the need for specific staining and examination under higher magnification, in order to rule out lichen simplex chronicus, and for the good response to treatment.

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