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Secondary Cutaneous Amyloidosis in Disseminated Superficial Porokeratosis: A Case Report

Disseminated superficial porokeratosis (DSP) is a rare cause of secondary cutaneous amyloidosis. An 83-year-old male patient showed an increase in both size and number of DSP lesions after contracting pulmonary tuberculosis. The DSP lesions of the patient consisted of numerous annular eruptions on both sun-exposed and sun-protected areas, which occurred over a period of 20 years. Multiple skin biopsies were taken from normal or lesional/ sun-exposed or sun-protected skin samples. Histopathologic examination included routine H&E stains, Congo red stains, thioflavin-T stains and anticytokeratin antibodies (AE1, AE3). And the results were as follows; 1) Positive staining with Congo red and thioflavin-T indicated an amyloid nature for the deposits, 2) confinement of the amyloid deposition just below the lesional epidermis (while sparing the neighboring uninvolved or distant normal skin) indicated some role of the lesional epidermis, and 3) positive staining with AE3 further indicated an epidermal origin-type II epithelial keratin-of the amyloid. We present a case of DSP with a local amyloid deposit, characterized by association of positive familial background, severe pruritus and pulmonary tuberculosis.

Key Words: *Amyloidosis; Porokeratosis, Disseminated Superficial; Tuberculosis; Keratin*

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INTRODUCTION

There are two types of localized cutaneous amyloidosis (LCA). Primary LCA (macular amyloidosis and lichen amyloidosus) occurs without preceding dermatoses, whereas secondary LCA is associated with a variety of inflammatory, hamartomatous or neoplastic skin disorders (1). Disseminated superficial porokeratosis (DSP), reported to be associated with LCA, is very rare (2-6)

The term "DSP" was introduced in 1937 by Andrew (7) to describe a clinical variant of Mibelli's porokeratosis. Thereafter, Chernosky and Freeman (8) drew attention to a possible actinic etiology of DSP and proposed the term disseminated superficial 'actinic' porokeratosis (DSAP). Nowadays the term DSAP is generally accepted in dermatology textbooks and the definition of DSAP is based on clinical and histological findings (9). The rashes are typically confined to sun-exposed areas, which show actinic induction and exacerbations (10). Although rare, dermal amyloid deposits were demonstrated in DSP or DSAP. Currently, six cases have been documented in the literature (2-6).

We studied here dermal amyloid deposits in a patient with DSP, which was aggravated after pulmonary tuberculosis.

CASE REPORT

An 83-year-old man was presented to our dermatology department on July 4, 1998 and reported that he had, multiple brown colored skin rashes for 20 years. Upon physical examination, numerous, 0.5-1.5 cm sized, annular and slightly raised maculopapules were distributed on the neck, chest, upper extremities and back (Fig. 1). The clinical features were typical of DSP, which was confirmed after subsequent skin biopsies. He complained of severe pruritus on the rashes, which were distributed throughout the sun-exposed and sun-protected areas. The patient's medical history revealed that sun exposure and seasonal influences were not aggravating factors, because the patient spent most of his time indoors and was not employed for 30 years after his retirement. It was further reported that the number and size of the rashes did not change over the last 20 years. In the beginning, the skin lesions appeared on the chest and upper extremities. One month prior to visiting our dermatology clinic, he was diagnosed with pulmonary tuberculosis at a private clinic and since then the skin lesions increased in number and size. He underwent sputum cytology with an AFB stain and chest radiography because of coughing and dyspnea.

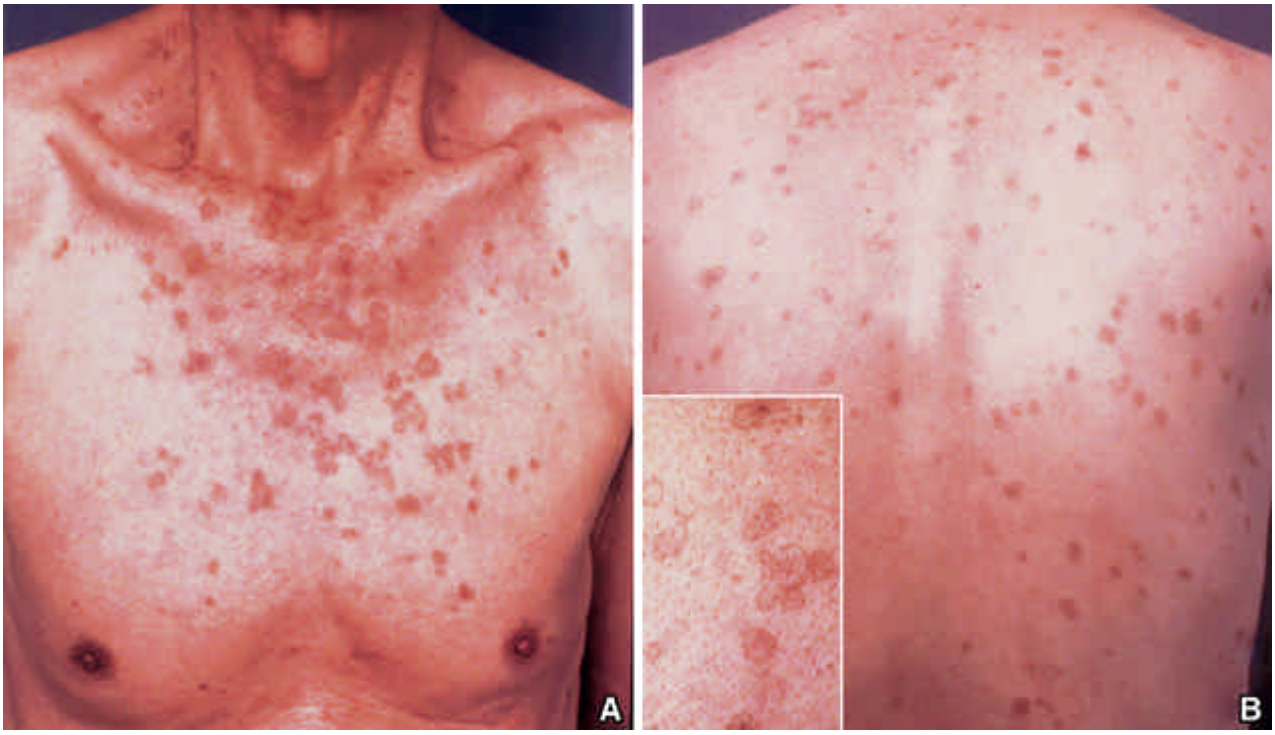

Fig. 1. Clinical features. A: Lesions on the neck and anterior chest, B: Lesions on the back and a close-up view (insert).

Sputum cytology was positive for *M. tuberculosis*. Antituberculous chemotherapy with isoniazid, rifampicin and ethambutol was initiated. Family history revealed that his daughter had similar skin lesions on the neck and upper extremities. Laboratory investigations did not detect any abnormal results in blood cell data, routine urine analysis and routine chemistry, including hepatic and renal function tests.

Four skin biopsy samples, taken from both normal and lesional sites of sun-exposed arm skin and sun-protected back skin, were subjected to routine histopathologic examination (Table 1). We checked for the presence of superficial dermal deposits in the normal or lesional skin specimens after staining with H&E, Congo red and thioflavin-T. Immunohistochemical stainings were performed on the 4 μM sections obtained from the paraffin blocks. The deparaffinized sections were incubated with two different monoclonal mouse IgG antibodies to human cytokeratins with different affinities for acidic and basic human keratin. AE1 (ScyTek, Utah, U.S.A.) recognizes the 56.5, 50, 48 and 40 kDa human cytokeratins of the acidic subfamily (type I epithelial keratin). AE3 (ScyTek, Utah, U.S.A.) recognizes the 65 to 67, 64, 59, 58, 56 and 52 kDa human cytokeratins of the basic subfamily (type II epithelial keratin). The sections were then processed by the avidin-biotin complex (ABC) method.

Table 1. Histopathological findings

	Cornoid lamella	Amyloid deposit
Biopsy specimens from		
Lesion, sun-exposed, arm	+	+
Lesion, sun-protected, back	+	+
Normal, sun-exposed, arm	−	−
Normal, sun-protected, back	−	−

Sections from the skin biopsies of the lesions showed typical findings of superficial porokeratosis, including cornoid lamella. Absent granular layer and dyskeratotic vacuolated keratinocytes were observed beneath the cornoid lamella. Dense aggregations of amorphous eosinophilic globular substances were observed in the papillary dermis, which were confined to areas just below the lesional epidermis (while sparing the neighboring uninvolved or distant normal skin), indicating some role of the lesional epidermis. This amorphous substance was clearly observed under Congo red stain (Fig. 2B). Subsequent multiple skin biopsies demonstrated that the lesional skin samples (sun-exposed or sun-protected) were positive for dermal amyloids while normal skins (sun-exposed or sun-protected) were negative (Table 1). The dermal amyloids were closely associated with the overlying lesional epidermis. Thioflavin-T stain (amyloid specific staining) under polarizing microscopy revealed bright yellow fluorescence of the dermal amyloid deposits (Fig. 2C). Although, immunohistochemical stainings were conducted using anticytokeratin antibodies both AE1 and AE3, only the AE3 showed intense staining of the dermal deposits (Fig. 2D).

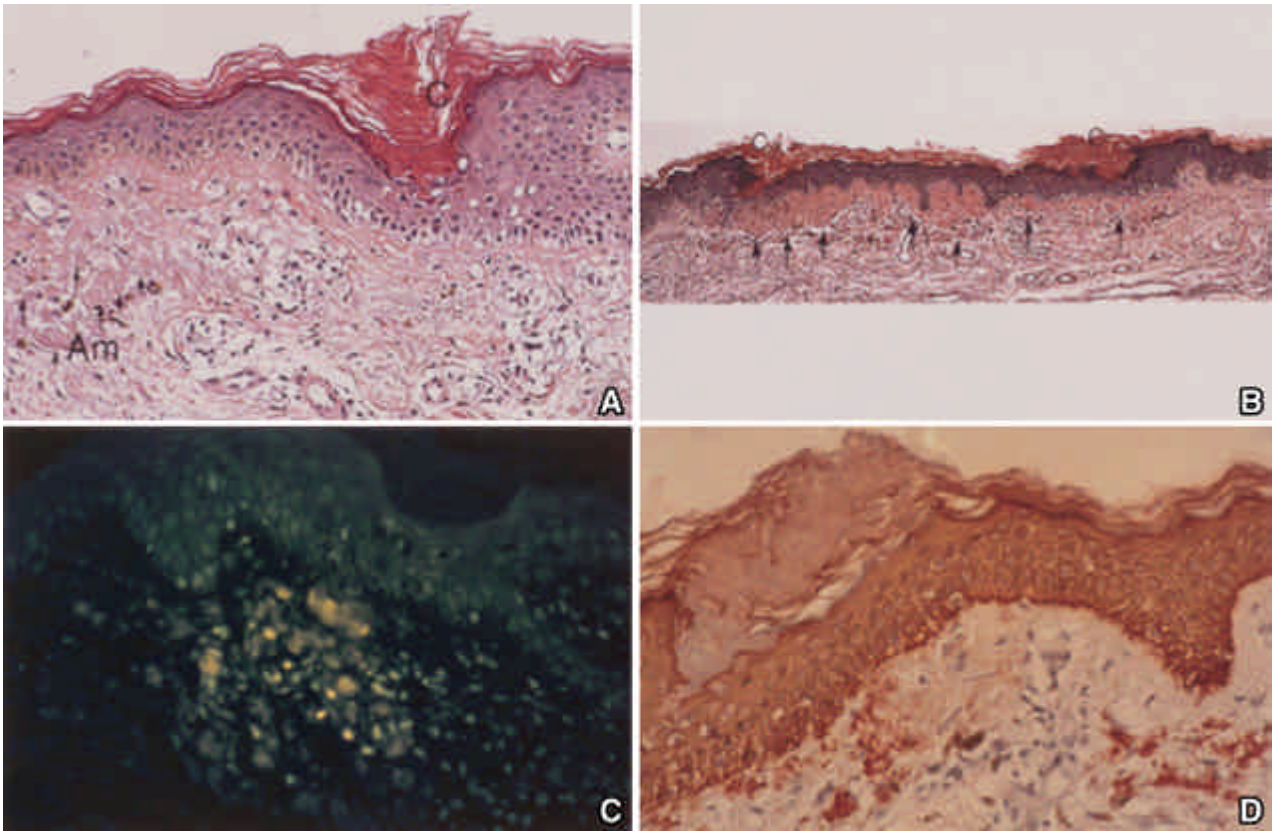

Fig. 2. Histopathological findings show characteristic features of porokeratosis and dermal amyloid deposits. **A:** Cornoid lamella (C) and dermal amyloid deposits (Am, arrows) are seen (H&E, ×200), **B:** Superficial dermal amyloid deposits (arrows) and cornoid lamellae (C), (Congo red, ×40), **C:** Dermal amyloid deposits under polarizing microscopy (Thioflavin-T stain, ×200), **D:** Positively stained epidermis and dermal amyloid deposits upon immunostaining using monoclonal antibody to human cytokeratin AE3 (×200).

These results indicated that the dermal deposits were amyloid that originated from the epidermis (type II keratin).

Topical corticosteroid treatment and systemic medication were effective in lessening the pruritus. To further ameliorate the pruritus, we attempted cryosurgery with a dry ice stick, which resulted in a decrease in the size and number of the lesions. Presently, the patient is being given oral medication (Cydraxin®; Hydroxyzine 60 mg #3) and follow-up treatment for the remaining pruritus, in the form of laser surgery and ongoing cryotherapy.

DISCUSSION

Histopathological evaluations revealed secondary LCA in the superficial dermis only beneath the porokeratotic epidermis. And the patient's amorphous deposits in the superficial dermis were amyloids of a secondary nature: 1) Positive staining with Congo red and thioflavin-T indicated an amyloid nature for the deposits, 2) confinement of the amyloid deposition, just below the lesional epidermis, (while sparing the neighboring uninvolved or distant normal skin) suggested a close relationship between the two processes, and 3) positive staining with AE3 further indicated an epidermal origin (type II epithelial keratin) of the amyloid. The result was consistent with the findings of Amantea et al. (5).

We prefer the term DSP (instead of DSAP) in the present case because our patient's porokeratotic lesions spread beyond the sun-exposed area and the patient's medical history had a lack of actinic induction and exacerbation. "DSAP" might be reserved for cases when the lesions are associated with sun exposure and confined to sun-exposed areas.

The mechanism by which DSP induces dermal amyloid deposits is not known. Piamphngstant et al. first suggested that the amyloid deposits in DSP might be derived from degenerated epidermal keratinocytes (2). Nowadays, a mutant keratinocyte clone, responsible for induction of the porokeratotic lesions, is presumed to somehow produce dermal amyloids (5). Necrotic epidermal cells (colloid bodies) might be transformed into amyloid by dermal macrophages and fibroblasts (11). In our immunohistochemical study, the dermal amyloid deposits was positive with AE3 stain, but negative with AE1. AE3 recognizes relatively high molecular weight human cytokeratin. We

Table 2. DSP with amyloid deposits: a summary of the reported cases

	Piamphongstant and Sittapairoachana (2) (1974)	Stefanato et al. (3) (1993)	Yasuda et al. (4) (1996)		Amantea et al. (5) (1998)	Demitsu and Okada (6) (1999)	Our Case (1999)
			Case 1	Case 2			
Age/Sex	51/F	32/F	63/M	60/M	72/M	63/M	88/M
Age onset	6th decade	4th decade	5th decade	6th decade	7th decade	adolescence	7th decade
Duration	7 years	1 month	20 years	2 years	3-4 years	n.d.	20 years
Pruritus	n.d.	none	slight	present	none	n.d.	severe
Family history	n.d.	negative	n.d.	n.d.	negative	negative	daughter
Treatment	n.d.	topical steroid etretinate	topical DMSO	topical DMSO topical steroid	n.d.	cryosurgery	topical steroid antihistamine cryosurgery
		↓	↓	↓		↓	↓
		not improved	improved	worsened		improved	improved

n.d., not described; DMSO, dimethyl sulfoxide

think that the dermal amyloid deposits in secondary LCA might have originated from relatively high molecular weight epithelial keratin (58-67 kDa).

No apparent triggering factors were noted in the patient except pulmonary tuberculosis, after which the lesions (DSP) spread rapidly. Immunosuppression by ultraviolet radiation, hematologic malignancies or chemotherapy after organ transplantation has been considered to be a causative factor of DSAP (12, 13). One of the patient's daughters had the same skin lesions (DSP) but the actinic factor was not thought to be a precipitating or aggravating factor. Pulmonary tuberculosis is a kind of chronic debilitating disease which decreases immunosurveillance. Also, anti-tuberculosis chemotherapy might suppress the cell-mediated immunity (14). Therefore, we assumed that the pulmonary tuberculosis in our case was causally associated with the spread of DSP. Since we treated the patient from the first visit with a topical steroid, systemic medications, cryosurgery and anti-tuberculosis therapy, we do not know which treatment was related to the improvement of skin lesions.

Pruritus is not a common clinical feature of DSP. Chernosky and Freeman reported that 37% of patients with DSAP showed symptoms of pruritus (8). In our case, the patient complained of severe pruritus.

Reported cases of DSP with local amyloid deposits are summarized in Table 2. The present case was characterized by the association of positive familial background, severe pruritus and pulmonary tuberculosis.

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