

ORIGINAL ARTICLE

Localized Cutaneous Amyloidosis Secondary to Porokeratosis: A Retrospective Histopathologic Study of 30 Patients

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Abstract. *Introduction.* Porokeratosis is a rare disorder of keratinization. The presence of amyloid deposits has been observed in inflammatory and tumoral skin diseases.

Objectives. The aim of this study was to determine the frequency of cutaneous amyloidosis in histology samples from various types of porokeratosis diagnosed in our department from 1988 to 2005.

Material and methods. Thirty patients were selected and 34 biopsies of lesions clinically and histologically compatible with porokeratosis were performed. Sections were stained with hematoxylin-eosin and thioflavin T.

Results. Amyloid deposits were observed in 11 biopsies from 9 patients. Most were women in their sixties, with disseminated superficial actinic porokeratosis that had begun at least 5 years earlier. No notable histologic differences were observed between porokeratosis specimens with and without amyloid deposits.

Conclusions. The coexistence of porokeratosis and amyloidosis is a rare occurrence but may be underdiagnosed. In our opinion, the advanced age of the patients and the chronic nature of the lesions would have been predisposing factors for amyloid deposition. The possibility of racial or genetic influences, however, cannot be ruled out.

Key words: porokeratosis, amyloid, secondary amyloidosis.

AMILOIDOSIS CUTÁNEA LOCALIZADA SECUNDARIA A POROQUERATOSIS. ESTUDIO HISTOPATOLÓGICO RETROSPECTIVO DE 30 PACIENTES

Resumen. *Introducción.* Las poroqueratosis son alteraciones de la queratinización poco frecuentes. La presencia de material amiloide se ha observado en dermatosis de etiología inflamatoria y tumoral.

Objetivos. Determinar la incidencia de amiloidosis cutánea en las muestras histológicas de distintos tipos de poroqueratosis diagnosticados en nuestro servicio entre 1988-2005.

Material y métodos. Se seleccionaron 30 pacientes y se realizaron 34 biopsias de lesiones compatibles clínica e histológicamente con poroqueratosis. Se realizaron tinciones con hematoxilina-eosina y tioflavina T en todas ellas.

Resultados. Se detectaron depósitos de amiloide en 11 biopsias que pertenecían a 9 pacientes. La mayoría eran mujeres en la sexta década de la vida, con la variante de poroqueratosis actínica superficial diseminada y con un tiempo de evolución superior a 5 años. No se encontraron diferencias histológicas significativas entre las biopsias de poroqueratosis con amiloide y sin él, a excepción del material anómalo.

Conclusiones. La coexistencia de poroqueratosis y amiloidosis es un hecho poco frecuente, posiblemente infradiagnosticado. Consideramos que la edad avanzada y la cronicidad de las lesiones serían factores predisponentes, sin poder descartarse una implicación racial o genética.

Palabras clave: poroqueratosis, amiloide, amiloidosis secundaria.

Introduction

Porokeratosis is a rare disorder of keratinization. Six different clinical forms are recognized, differentiated by the number, size, and site of the lesions, and also by whether the lesions have been exacerbated by exposure to the sun. The 6 forms of porokeratosis are classical porokeratosis (also known as Mibelli porokeratosis), disseminated superficial actinic

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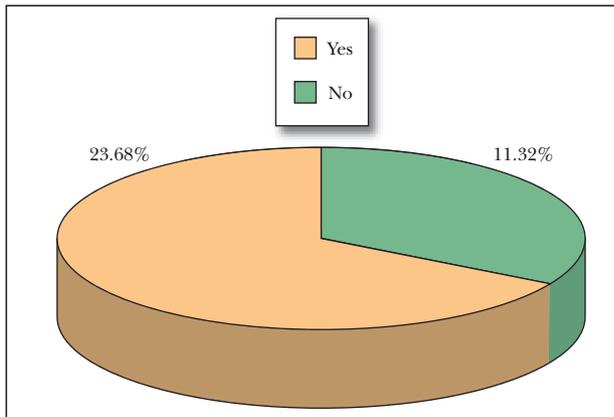


Figure 1. Percentage of patients with amyloidosis in porokeratosis lesions.

porokeratosis, disseminated superficial porokeratosis, linear porokeratosis, porokeratosis palmaris, plantaris et disseminata, and punctate porokeratosis.¹ All 6 forms are characterized by the presence of a column of parakeratotic cells known as the cornoid lamella.

Amyloidosis refers to the deposition of abnormal extracellular material with common physical and chemical properties, spatial configuration, and staining properties.²

Amyloid deposits have been observed in inflammatory dermatoses and skin tumors,³ such as seborrheic keratosis,⁴ basal cell carcinomas,⁵ trichoepitheliomas,⁶ chronic cutaneous lupus erythematosus,⁷ and porokeratosis.⁸ The amyloid deposits in these conditions are classified as secondary localized cutaneous amyloidosis, despite the fact that the etiopathogenic mechanism is the same as that for macular and lichenoid primary cutaneous amyloidosis. In the macular and lichenoid variants, the abnormal material comes from degenerated keratinocytes.⁹

Objectives

The aim of this retrospective study was to identify the presence of amyloid deposits in histologic samples from patients with different types of porokeratosis, diagnosed in our hospital over a period of 18 years (1988 through 2005), with a view to establishing epidemiologic, clinical, and histologic factors related to the presence of these deposits. We also compared our results with those obtained in other studies.

Given the absence of similar studies that included series of patients, reference is made to isolated case reports.

Materials and Methods

A total of 30 hospitalized or outpatient subjects were selected for the study, and 34 excisional biopsies were performed

on lesions clinically compatible with different types of porokeratosis. All the biopsies included perilesional healthy skin. The samples were stained with hematoxylin-eosin and thioflavin T. The diagnosis of porokeratosis was based on clinical characteristics (number, size, and site of the lesions) and histologic criteria; the presence of cornoid lamellae was considered to be a diagnostic requisite.

Complementary tests performed on all the patients included biochemistry, complete blood count, coagulation, urinalysis, protein profile, immunoglobulin and complement measurement, and erythrocyte sedimentation rate.

Results

There were 21 women (70%) and 9 men (30%) in the sample of 30 patients, with a mean age of 55.04 years (range, 20–83 years). Amyloid deposits were observed in 11 of the 34 biopsies (32.35%) stained with thioflavin T (Figure 1). These biopsies were from 9 of the 30 patients (30%) in the overall sample. The Table shows the epidemiologic, clinical, and histologic data for the patients.

Most of the patients with amyloid deposits were in the age bands 61–70 years and 71–80 years, with a mean age of 66.54 years. There was a slight female predominance (55%), with a mean age of 63.72 years compared to 70.15 years for men. Prevalence was higher among women except in the 61–70 and 81–90 age bands (Figure 2). The mean age of patients without amyloid deposits was 51.74 years.

For the porokeratosis lesions associated with amyloidosis, time since onset was greater (mean, 8.84 years) than in the overall sample (mean, 5.25 years) or in patients without secondary cutaneous amyloidosis (mean, 4.25 years).

The most frequent form of porokeratosis in the overall sample was disseminated superficial actinic porokeratosis (20 patients), and this was also true of the group of patients with secondary cutaneous amyloidosis (Figure 3). Although 7 of the biopsies from the overall group corresponded to Mibelli porokeratosis, none of these biopsies revealed abnormal deposits.

The most frequent sites of the lesions in disseminated superficial actinic porokeratosis and disseminated superficial porokeratosis were the limbs and trunk. No abnormal deposits were observed in any of the facial or genital lesions corresponding to Mibelli porokeratosis. Amyloid deposits were found in both sun-exposed and sun-protected lesions, and also in both pruriginous and asymptomatic lesions. Other dermatoses in the patients in the overall sample were as follows: stasis dermatitis (5 patients), actinic keratosis (1 patient), dermatomyositis (1 patient), pemphigus vulgaris (1 patient), psoriasis (1 patient), and livedo reticularis (1 patient). None of these patients had amyloid deposits in their porokeratosis lesions.

Table. Patient Clinical, Epidemiologic, and Histopathologic Data

Patient	Age, y	Sex	Time Since Onset	Clinical Type	Lesion Site	Exposure to Sun	Symptoms	Site of Deposit
1	68	M	10 y	DSP	Limbs and trunk	No	Pruritus	Dermis
2	59	F	20 y	DSAP	Lower limbs	Yes	No	Proximal dermis, distant from cornoid lamella
3	73	F	10 y	DSAP	Lower limbs	Yes	Pruritus	Dermis
4	74	F	–	DSAP	Upper and lower limbs	Yes	Pruritus	Dermis
5	65	M	4 y	DSP	Trunk and limbs	No	No	Dermis
6	48	F	5 y	LP	Axilla	No	No	Dermis
			35 y	DSAP	Upper and lower limbs	Yes		Dermis and basement membrane
7	66	M	6 mo	DSAP	Lower limbs	No	Pruritus	Dermis
8	69	F	10 y	DSAP	Upper and lower limbs	Yes	No	Cornoid lamella and dermis
9	83	M	20 y	DSP	Trunk and limbs	No	Mild pruritus	2 biopsies Dermis

Abbreviations: DSAP, disseminated superficial actinic porokeratosis; DSP, disseminated superficial porokeratosis; F, female; LP, linear porokeratosis; M, male.

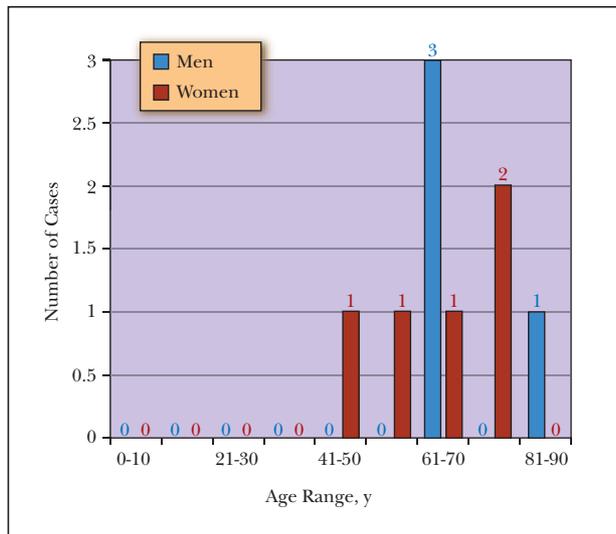


Figure 2. Distribution by age and sex of patients with amyloidosis in porokeratosis lesions.

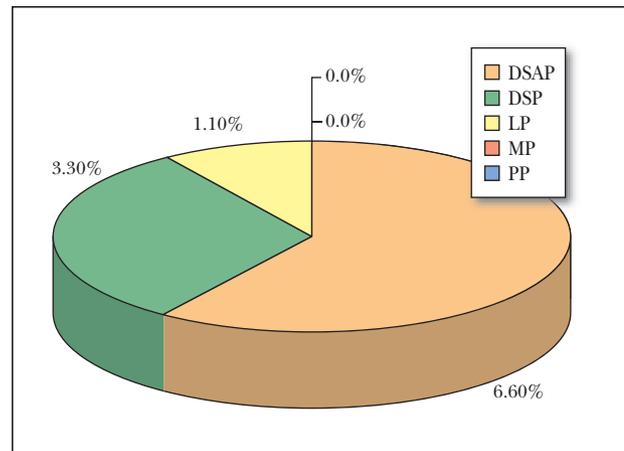


Figure 3. Types of porokeratosis with amyloid deposits. DSAP indicates disseminated superficial actinic porokeratosis; DSP, disseminated superficial porokeratosis; LP, linear porokeratosis; MP, Mibelli porokeratosis; PP, punctate porokeratosis.

One patient had 2 types of porokeratosis (disseminated superficial actinic porokeratosis and linear porokeratosis), with abnormal deposits in both types of lesion. In 1 patient with disseminated superficial porokeratosis, 2 lesions were biopsied (from sun-exposed and sun-protected areas), with amyloid deposits confirmed in both lesions.

In the 34 biopsies performed, hematoxylin-eosin staining revealed the cornoid lamellae and underlying dyskeratosis and hypogranulosis. The presence of a predominantly

mononuclear inflammatory infiltrate was a characteristic finding. In 48% of cases, the infiltrate—located in the upper dermis, and, more abundantly, below the cornoid lamella—was significant. In the other patients, the infiltrate was minimal and was almost always associated with the parakeratotic column. There was basal cell degeneration and vacuolization in 91% of the biopsies, and pigment incontinence and melanophages were present in 84% of the biopsies. No significant differences were observed in the

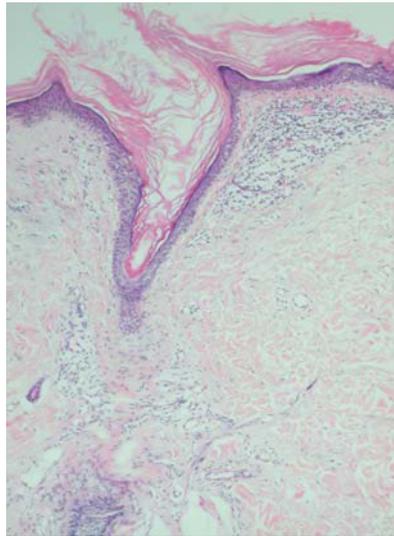


Figure 4. Deposits of hyaline and eosinophilic material in the upper dermis close to the cornoid lamella (hematoxylin-eosin, original magnification $\times 100$).

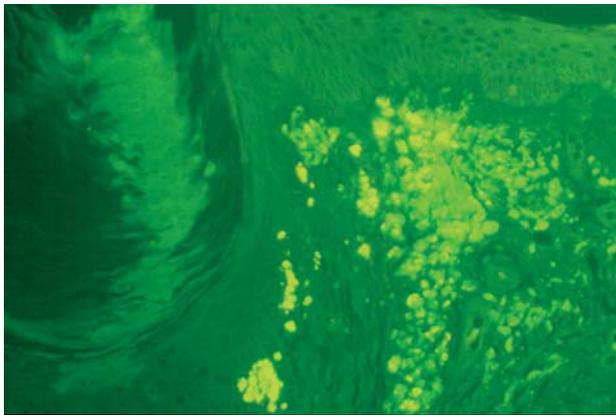


Figure 5. Fluorescence of the amyloid deposits in the papillary dermis (thioflavin T, original magnification $\times 200$).

density of the inflammatory infiltrate, basal cell vacuolization, and pigment incontinence between the cases with and without amyloid deposits.

In 6 of the samples stained with hematoxylin-eosin, it was possible to identify the amyloid as accumulations of acellular, eosinophilic, hyaline material (Figure 4), and this was confirmed using thioflavin T. The abnormal deposits were found in the papillary dermis in the 11 biopsies (Figure 5); in 1 of the biopsies, deposits were also observed in the cornoid lamella, and in another biopsy also at the dermal-epidermal junction. In all cases, the deposits were associated with and close to the parakeratotic column, although in 1 sample, they were observed in the center of the lesion, at some distance from the cornoid lamella. No deposits were identified in perilesional healthy skin.

Treatment was not determined by the presence or absence of amyloidosis, as specific staining was done later in some

cases. Nor were differences observed in regard to the course of the lesions with and without amyloidosis. Finally, of the 26 patients whose lesions could be followed up, none developed malignant changes.

Discussion

The presence of amyloid deposits in porokeratosis lesions was first described in 1974.⁸ Since then, we have found 24 cases in the literature.^{8,10-24} Most cases were in men^{8,10,13-21,23} aged over 60 years and of Asian origin. Disseminated superficial porokeratosis was the most frequently reported variant in these cases.¹⁴⁻¹⁸ Nonetheless, 8 of the reported cases referred to Mibelli porokeratosis.^{10,12,13,21,24}

Gender differences in our series of patients can be explained by the overall composition of the sample—with a clear female predominance—and also by the fact that the most frequent variant of porokeratosis among our patients—disseminated superficial actinic porokeratosis—is reported mostly in women.

The mean age for the group of patients with amyloid deposits was higher than that of the overall group, although this difference was not statistically significant. Our data, in this respect, are similar to those described for previous cases, in which the reported mean age was over 60 years.

Time since onset of the lesions was greater in patients with secondary amyloidosis, although this difference was not statistically significant. However, the fact that amyloid developed in some cases of porokeratosis of recent onset, both in our series and in other studies,^{14,15} would suggest that other factors are implicated.

Noteworthy is the fact that amyloid deposits were not detected in patients in our series with Mibelli porokeratosis, in contrast to other studies, possibly because our patients were younger and so the lesions were more recent.

Amyloid deposits were observed in lesions in both sun-exposed and sun-protected areas. Since most of the subjects were elderly patients with disseminated superficial actinic porokeratosis, it is thought that sunlight played a role in the development of the disease. However, abnormal deposits have been reported in lesions in both sun-exposed and sun-protected areas in the same patient.^{17,19,22} Although the sun-exposure argument has been defended by some authors for other forms of secondary cutaneous amyloidosis,^{25,26} other authors found no relationship.^{4,5}

It is thought that epidermal damage in pruriginous lesions may play a role in the development of secondary cutaneous amyloidosis,²⁷ although, in our series, this cannot be considered a determining factor; likewise with the cases previously described, given that amyloidosis has been observed both in pruriginous lesions^{14,16,19,20} and in asymptomatic lesions.^{5,17,22}

A genetic or racial factor has been put forward as a possible cause of the disease, given that a large proportion of the patients are of Asian origin.^{8,11-13,16,18-21,24} Amyloidosis secondary to porokeratosis has also been reported in 2 elderly siblings.²⁴

As found in other studies, amyloid deposition in our patients is likely to be secondary to epidermal degeneration of the primary lesion. This conclusion is also supported by the fact that abnormal deposits do not occur in other dermatoses and are restricted to lesions with no involvement of adjacent healthy skin.

The histologic findings in our series of patients did not differ from the other reported cases, where the typical site of the amyloid deposits was in the papillary dermis underlying the cornoid lamella. Deposits are less frequently encountered within the lamella,^{18,22} or in central areas of the lesions.¹⁶ Although it is thought that the presence of a minimal inflammatory infiltrate²⁴ with abundant melanophages and pigment incontinence²⁸ might be useful signs in hematoxylin-eosin-stained samples to suggest the presence of secondary amyloidosis, we found no differences in this respect.

On the basis of the results from our series of patients, there appears to be an association between porokeratosis and secondary cutaneous amyloidosis. The association may occur frequently, but may go underreported because the amyloid deposits may not be evident using the usual stains¹⁷ and because clinical findings are not apparent. It would seem that the epidermal degeneration occurring in this form of amyloidosis is more frequently found in elderly patients and in long-standing lesions.

Conflicts of Interest

The authors declare no conflicts of interest.

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