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Original Article

Clinical pattern of primary cutaneous amyloidosis in Hong Kong Chinese

香港華人中的原發性皮膚澱粉樣變之臨床表現

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Objective: To evaluate and assess patients with primary cutaneous amyloidosis with regard to sex, age and clinico-pathologic features in the local population. ***Design:*** Retrospective case study. ***Setting:*** Social hygiene clinic in Tuen Mun, New Territories, Hong Kong. ***Patients:*** Chinese patients with a clinical +/- histological diagnosis of primary cutaneous amyloidosis: lichen amyloidosis and macular amyloidosis. ***Results:*** A total of 11 Chinese patients with primary cutaneous amyloidosis were successfully recruited at the Tuen Mun Social Hygiene Clinic from July to December 2008. Mean age of patients was 55.8 years with a male to female sex ratio of 1.2 to 1. Most patients (63.6%) presented after 40 years old (43-67 years old). The average age of onset was 45.3 years old (16-67 years old). Pruritus was the most common complaint. Limbs and upper back were most frequently affected. About half of the patients (45.5%) reported a significant reduction of itch (≥50% reduction in severity) with topical steroid with/without salicylic acid or oral antihistamine. However, there was no improvement in pigmentation or skin texture. ***Conclusion:*** Clinicians should bear in mind the possibility of primary cutaneous amyloidosis when encountering middle age patients presenting with localized pruritic skin lesions on limbs or upper back. Simple treatments with topical steroid with/without salicylic acid can usually ameliorate pruritus though improvement in pigmentation and skin texture is not promising.

目標：對原發性皮膚澱粉樣變的本地病患進行關於性別、年齡及臨床病理特徵的評估考究。**方法：**回顧性案例研究。**背景：**香港新界屯門區社會衛生科診所。**患者：**包含苔蘚型及斑狀型的原發性皮膚澱粉樣變之臨床或再加上組織學診斷的華人患者。**結果：**二零零八年七月至十二月期間，在屯門社會衛生科診所共招募得十一位原發性皮膚澱粉樣變的華人患者。患者平均年齡為55.8歲，男女比例為1.2比1，大部份患者（63.6%）在四十歲後發病（43-67歲）。縱覽全部案例（16-67歲）平均發病年齡為45.3歲。瘙癢為最常見的症狀，而患處則多見於四肢及上背部。大約一半患者（45.5%）在使用外用類固醇激素再加水楊酸或抗組織胺治療後，瘙癢方面得

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到大幅改善（嚴重程度減卻≥50%）。反之，色斑或皮膚斑理問題則沒有改善。**結論：**當醫生遇見四肢或上背部有局部痕癢皮膚的中年患者時，必謹記原發性皮膚澱粉樣變的可能。簡單的外用類固醇激素或再加上水楊酸治療多能緩和瘙癢症狀，但色斑及皮膚斑理的改善則不予樂觀。

Keywords: Lichen amyloidosis, macular amyloidosis, primary cutaneous amyloidosis

關鍵詞：苔蘚型原發性皮膚澱粉樣變，斑狀型原發性皮膚澱粉樣變，原發性皮膚澱粉樣變

Introduction

Primary cutaneous amyloidosis (PCA) is associated with the deposition of amyloid fibrils in a previously apparently normal skin without associated deposits in internal organs. The pathogenesis of PCA remains unknown. Amyloid deposits in PCA may be initially derived from cytokeratin, possibly after keratinocyte death as a result of apoptosis.[1] The three common types are lichen amyloidosis, macular amyloidosis and biphasic amyloidosis.[2] It is an uncommon condition and rarely encountered in primary care. It mainly affects Southeast Asians, Middle Easterners, Chinese and South Americans.[3,4] The aetiology remains unknown although genetic predisposition and racial factors are thought to be contributing factors.[5]

Lichen amyloidosis is the most common form of primary cutaneous amyloidosis. It was first described by Gutmann in 1928 as amyloidosis (sic), localis cutis nodularis et disseminate, and later by Freudenthal in 1930 as lichen amyloidosis.[6] The characteristic feature is the presence of multiple discrete hyperkeratotic scaly papules and plaques. It causes cosmetic disfigurement and sometimes itching that could be significant (Figures 1 & 2).[2]

Macular amyloidosis was first described by Palitz and Peck in 1952.[7] The characteristic feature is a ripple pattern of hyper-pigmentation. It is usually pruritic but it can be asymptomatic. The lesions are hyper-pigmented, either in a confluent manner or ripple-pattern. The common sites are the upper back, followed by extensor surfaces of the extremities (Figure 3).[2]

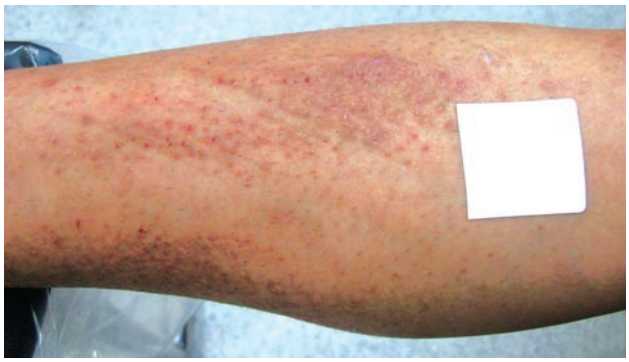

Figure 1. Lichen amyloidosis over the anterior aspect of shin.

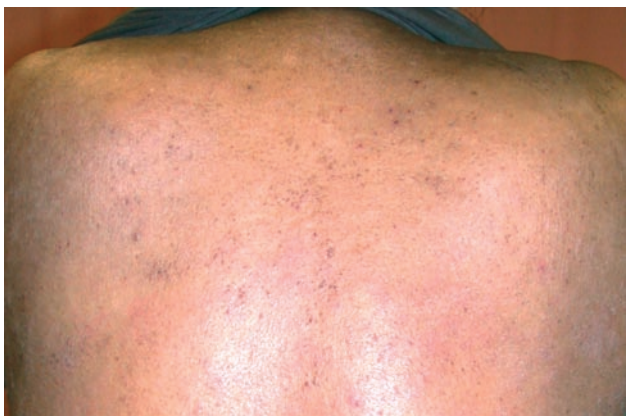

Figure 2. Lichen amyloidosis over the upper back.

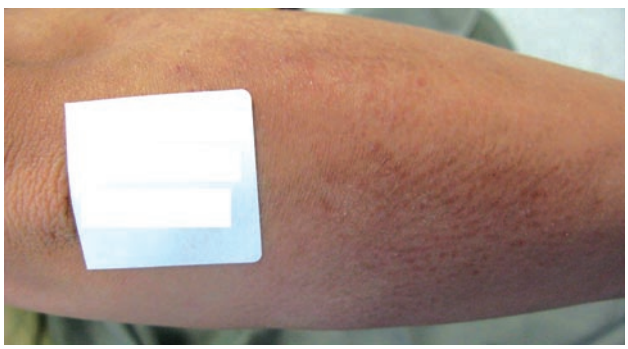

Figure 3. Macular amyloidosis over the forearm.

Biphasic amyloidosis is the presence of both forms in the same patient.[2]

Methods

Eleven Chinese patients with a clinical diagnosis of one or more forms of primary cutaneous amyloidosis were recruited at Tuen Mun Social Hygiene Clinic during a period of six months from July to December 2008. They satisfied the criteria of lichen amyloidosis or macular amyloidosis either by histological examination or assessment by two or more dermatologists. The clinical criterion for lichen amyloidosis is the presence of multiple discrete hyperkeratotic, firm, non-elastic, non-tender, scaly, closely set, match-head to pea-sized, skin-coloured or brownish, dome-shaped or hemi-spherical papules;[8] for macular amyloidosis is the presence of hyper-pigmented, ripple-patterned patches of the skin with closely aggregated grayish brown macules; for biphasic amyloidosis is the presence of both in the same patient. The histological criterion is the presence of amyloid deposits restricted to the upper dermis. Discordance between clinical assessment and histological examination was reconciled by the review of histological report and agreement between the investigators.

The patients' demographic and clinico-pathological features were recorded and analyzed. These included history on their age of onset, relevant family history, past medical and dermatological history, and symptomatology. During their visit within the study period, a comprehensive cutaneous and systemic examination was carried out. Relevant laboratory tests including complete blood picture with differential count, liver and renal function test, anti-nuclear antibody, anti-DNA, immunoglobulin pattern and a skin biopsy were done whenever appropriate.

Results

During the 6-month period from July to December 2008, a total of 11 patients with primary cutaneous amyloidosis were identified at Tuen Mun Social Hygiene Clinic. Six were male and five were female. Their mean age was 55.8 (range, 38-70) years old and all of them were Hong Kong Chinese. About 2/3 of the patients (7 patients) presented after 40 years old (43-67). The average age of onset was 45.3 years old (16-67 years old). Six patients reported a history of regular scratching of the affected area. Concurrent eczema was also present in 60% of cases. Two patients had a family history of primary cutaneous amyloidosis. For patient number six, his father and two out of five sisters were involved. For patient number eleven, her mother and four out of six siblings were involved. Patient demographics and other relevant history are listed in Table 1.

Clinically, nearly all patients complained of itch. The itch was worsened by hot weather in 72.7% of cases and relieved by topical steroid. On detailed questioning, six patients recalled a prolonged history of pruritus before the presence of lesions (Patient no. 4, 5, 7, 8, 9, 11). Among them, four patients had chronic eczema. On clinical examination, four patients had macular lesions, another four had papular lesions and three had both types of lesions. The distribution was mainly over the extensor surfaces of the limbs and upper back. Skin biopsy was performed in four patients and confirmed the diagnosis of lichen amyloidosis. The rationale for performing skin biopsy was not mentioned in the medical records. So, the decision of performing skin biopsy may be due to clinician's preference or to exclude other skin conditions like chronic eczema. The clinico-pathological features of patients are shown in Table 2.

All patients were offered topical steroid +/- salicylic acid for symptomatic relief. One patient was put on acitretin 25 mg daily in addition to topical treatment. Nine patients had decreased itch. Among them, five patients had decreased severity of itch of 50% or more. Three had flattening of papules, including the patient receiving acitretin. Four had subjective decrease in pigmentation but the decrease was not significant (Table 3). None of the patients developed complications from topical or systemic treatment.

Discussion

In this study, 11 patients satisfied the criteria of lichen amyloidosis or macular amyloidosis either by histological examination or assessment by two or more dermatologists. The disease affects both sexes with a male to female ratio of 1.2:1. Only two patients in our study reported a family history of lichen amyloidosis.

Pruritus is the major complaint of patients and this may be worsened by hot weather or mood. In our patients, topical steroids provide good symptomatic relief. There was also some improvement in reducing the thickness and hyper-pigmentation of lesions.

Similar studies on primary cutaneous amyloidosis were carried out in Singapore, South America and Taiwan. The clinical features of primary cutaneous amyloidosis in different areas are summarized in Table 4. In the Singaporean and South American studies, there was female predominance with a male to female

Table 1. Patient demographics and other relevant history

Patient	Sex/ Age	Age of onset	Duration (Years)	Alleged precipitating factor(s)	Family history	Concomitant skin disease	Relevant medical history	Pre-referral diagnosis
1	M/70	67	3	Rubbing & scratching	–	–	HT, CVA, PPU, gout	Eczema
2	M/53	43	10	–	–	Eczema	–	Multiple warts
3	M/69	56	13	–	–	–	–	Eczema
4	M/59	55	4	Scratching	–	–	BPH	LA
5	M/62	50	12	Scratching	–	Scalp eczema	–	Thickened skin
6	M/61	18	43	–	+(a)	Eczema	HT, IHD, gout	Red dots
7	F/55	53	2	Scratching	–	Eczema	HT, DM	Eczema
8	F/62	57	5	–	–	LSC	Thyrotoxicosis	Eczema
9	F/42	38	4	Scratching	–	Atopic eczema	–	LA
10	F/43	34	9	–	–	–	–	Keratinized papules
11	F/38	27	11	Scratching	+(b)	Atopic eczema Allergic rhinitis	–	Generalized itchy skin

BPH=benign prostate hypertrophy; CVA=cerebrovascular accident; DM=diabetes mellitus; HT=hypertension; IHD=ischaemic heart disease; LA=lichen amyloidosis; LSC=lichen simplex chronicus; PPU=perforated peptic ulcer
(a) father, 2 out of 5 sisters were involved; (b) mother, 4 out of 6 siblings were involved

ratio of 1:3. In the Taiwanese study, it was carried out at the Taipei Veterans General Hospital and most of the patients were male. This could account for the male predominance of the study. The peak incidence in different studies was different but most patients presented after 30 years old. The duration of illness varied a lot and confirmed the chronicity of this disease. Family history of primary cutaneous amyloidosis could be found in the South American, Taiwanese and Hong Kong studies. Most cases were sporadic but the positive family history suggested that genetic component might play a role in the pathogenesis.

Table 2. Patient's clinicopathological features

Patient	Symptoms	Provoking factors	Relieving factors	Lesion morphology	Distribution	Laboratory investigation	Skin biopsy	Clinical type of PCA
1	Pruritus	Hot weather	Cold weather, topical steroid	Macular	Whole back	–	LA	MA
2	Pruritus	Hot weather	Topical steroid	Macular + papular	Forearms, shins, calves	–	–	BA
3	Pruritus	–	–	Papular	Bilateral shins	Blood tests: normal	LA	LA
4	Pruritus	Winter, scratching	Topical steroid	Papular	Forearms, shins	–	–	LA
5	Pruritus, cosmetic	Hot weather	Topical steroid	Papular	Left shin	–	–	LA
6	Pruritus	Hot weather, mood	Topical + oral antihistamines, happy mood	Papular	4 limbs	–	–	LA
7	Pruritus	Hot weather, mood	Good DM control	Macular	4 limbs + back	–	–	MA
8	–	–	–	Macular	Right shin	–	LA	MA
9	Pruritus	Hot weather, mood	Cold weather	Macular + papular	Upper back, bilateral upper arms	–	LA	BA
10	Pruritus	Seafood	Topical steroid	Macular	RUL + bilateral shins	–	–	MA
11	Pruritus, cosmetic	Winter	–	Macular + papular	Whole back, bilateral upper arms + forearms, extensor surfaces of legs	IgE=133(↑)	–	BA

BA=biphasic amyloidosis; DM=diabetes mellitus; LA=lichen amyloidosis; MA=macular amyloidosis; PCA=primary cutaneous amyloidosis; RUL=Right upper limb

Table 3. Patient's treatment and progress

Patient	Topical treatment	Systemic treatment	Surgery	Clinical progress			
				Pruritus	Lesions	Pigmentation	Xerosis
1	TS	OA	–	Reduced by 89-90%	Papules flattened	Subjective improvement	Same
2	TS + SA	OA	–	Reduced by 30%	Same	Subjective improvement	Same
3	TS + SA	Acitretin 25 mg daily, OA	–	Same	Papules flattened	Same	Same
4	TS + SA	OA	–	Reduced by 50%	Papules flattened	Same	Same
5	TS + SA	OA	–	Reduced by 50%	Same	Same	Decreased
6	TS + SA	OA	–	Marked improve	Same	Same	Same
7	TS + SA	OA	–	Reduced by 30-40%	Same	Same	Same
8	TS + SA	–	–	Reduced by 10%	Same	Subjective improvement	Subjective improvement
9	TS	OA	–	Reduced by 70%	Same	Reduced by 60-70%	Same
10	TS + SA	–	–	Reduced by 20-30%	Same	Same	Same
11	TS + C	OA	–	Progressive worsening	Progressive worsening	Progressive worsening	Progressive worsening

C=crotamiton cream; OA=oral antihistamine; SA=salicylic acid; TS=topical steroid

Table 4. Clinical features of primary cutaneous amyloidosis in different areas

Clinical features	Singapore[3]	South America[4]	Taiwan, ROC[8]	Hong Kong
Case number	265	604	794	11
Sex ratio (M:F)	1:3	1:3	2:1	1.2:1
Peak incidence (age interval, years)	30-50	35-44	51-60	51-60
Duration of illness (years)	1-30	NA	1-40	2-43
Frequency of clinical type (%)				
LA	80	32.15	67	36.4
MA	6	35.71	8	36.4
BA	14	15.71	25	27.2
Family history (%)	ND	33.86	7.06	18

LA=lichen amyloidosis; MA=macular amyloidosis; BA=biphasic amyloidosis; ND=no data

As primary cutaneous amyloidosis is an uncommon condition, primary care physicians may have a low index of suspicion. In our study, only two patients were diagnosed correctly by referring physicians, the other nine patients were labeled as eczema, multiple warts or keratinized papules. Clinicians should bear in mind this diagnosis when encountering patients presenting with localized pruritic skin lesions on limbs or upper back.

The major limitation of this study is the small patient number and that it was carried out at one centre only. Furthermore, patients with asymptomatic macular amyloidosis on their back may not seek medical opinion.

To throw more light on primary cutaneous amyloidosis affecting Hong Kong Chinese, we propose a need for conducting a prolonged cohort prospective multi-centre study on the epidemiology, treatment efficacy and impact on quality of life.

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