

## Case Report

# Photodistributed macular amyloidosis presenting as diffuse facial pigmentation mimicking melasma: the surprising reveal

## 驚奇皮案：光照部位的斑疹型澱粉樣變表現為疑似黃褐斑的瀰漫性面部色斑

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Primary cutaneous amyloidosis is a chronic pruritic disorder with characteristic amyloid deposits in the papillary dermis. The manifestations of primary localised cutaneous amyloidosis (PLCA) are usually confined to the skin. The aetiopathogenesis of PLCA has not been clearly elucidated. We report a patient who developed PLCA after a short intense period of sun-exposure which we postulate that it may be the triggering factor in the development of macular amyloidosis.

原發性皮膚型澱粉樣變是一種慢性瘙癢疾病，其特徵為乳突真皮層中的澱粉樣蛋白沉積。原發局部性皮膚型澱粉樣的臨床表現多局限於皮膚，而其成因病理至今仍未能清楚闡釋。我們報告一名原發局部性皮膚型澱粉樣變患者，在短暫強烈日照後發病，從而假定其為斑疹型澱粉樣變的其中一個可能發病誘因。

**Keywords:** Amyloidosis, photodistributed, pigmentation

關鍵詞：澱粉樣變，光照部位的，色斑

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### Introduction

We report a patient with an unusual variant of macular amyloidosis who had diffuse homogenous hyperpigmentation involving the face and neck. The skin biopsy in this patient revealed globular amyloid deposits in the papillary dermis. There was no systemic involvement. The

rash in this patient could easily have been confused with hyperpigmentation caused by cutaneous inflammation, drugs and endocrine disorders.

### Case report

A 53-year-old lady of Indian origin presented to the National Skin Centre, Singapore with a five-year history of evolving dark patches over her face. She distinctly recalled developing a rash over her face after significant sun-exposure without wearing any sunblock while on holiday in Venice. Over the next few years the skin over her face and neck gradually darkened. There was no history of stinging, itching, burning or pain, nor had there been any preceding redness. There was no history of photosensitivity. She described no family history of similar pigmentary problems. She had been taking atenolol for the past three years and premarin (conjugated oestrogens) which she had been on for four years. The pigmentation preceded the commencement of the drugs. She did not take any supplements except for cod liver oil and multivitamins. She gave no history of contactants and denied constant rubbing of her face. There was no history of atopy and she was otherwise well.

Clinical examination revealed Fitzpatrick skin type V. There were patches of ill-defined, pigmented areas over her forehead, cheeks and chin (Figures 1, 2, 3). Areas of sparing were noted over the submental region, postauricular area and upper lip. There was no macroglossia, hepatosplenomegaly or purpura. There was no darkening of the palmar creases. At this point the differentials of lichen planus pigmentosus, melasma, drug-induced pigmentation and phototoxic contact dermatitis were considered.

A skin biopsy was performed which showed superficial and perifollicular infiltrates of lymphocytes associated with focal basal vacuolar alteration confined to the hair follicle



**Figure 1.** Diffuse brown to black pigmentation seen over the face and neck of the patient.



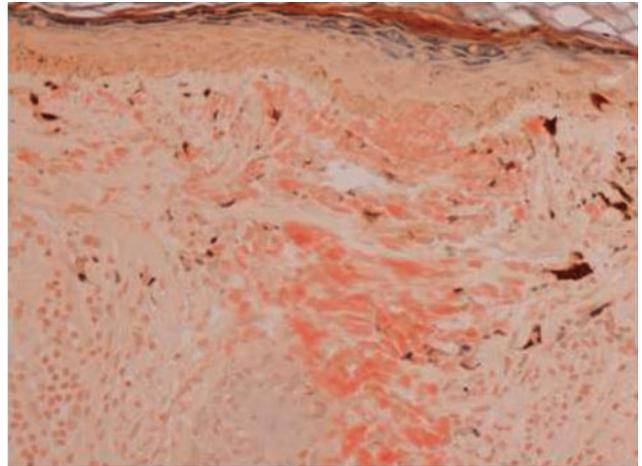
**Figure 2.** Brown to black patchy pigmentation over the forehead, nose, cheeks and chin with sparing of the upper lip, submental area and postauricular areas. The scalp was uninvolved.

epithelium (Figure 4). There was marked melanin incontinence and increased number of melanophages in the upper dermis. Aggregates of eosinophilic globules were seen in the papillary dermis which stained positively with Congo red and showed apple green birefringence on

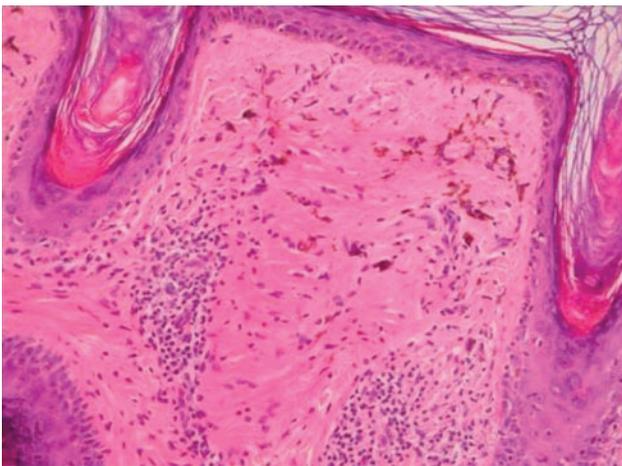
polarised light confirming the presence of amyloid (Figures 5 and 6). The areas of interface dermatitis were largely confined to the hair follicles and did not correspond to the areas of amyloid deposition. There was no amyloid seen around dermal blood vessels.



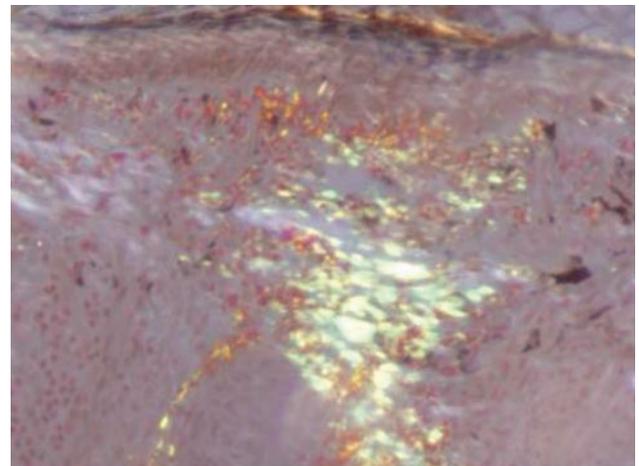
**Figure 3.** Close up view of the brownish black pigmented patches over the cheeks extending onto the ears.



**Figure 5.** Biopsy specimen from the face of the patient showing globular aggregates in the upper dermis staining bright red with Congo red (Congo red stain, Original magnification x 200).



**Figure 4.** Skin biopsy from the face of the patient showing pigmentary incontinence, melanophages in the papillary dermis, superficial dermal lymphocytic infiltrate and eosinophilic globules in the papillary dermis. Basal vacuolar alteration is confined to the follicular epithelium (H&E, Original magnification x 100).



**Figure 6.** These globular aggregates show positive apple-green birefringence when stained with Congo red, under polarised microscopy (Congo red stain with polarised light, Original magnification x 200).

## Discussion

In our patient the skin lesions were characterised by widespread homogenous dark brown pigmented patches over the face and neck. Histopathologically the amyloid deposits were limited to the subepidermal area arranged in eosinophilic globules in a linear fashion with no involvement of the adnexal structures, blood vessels and nerves to suggest systemic amyloidosis. The clinical features were unique in that the discolouration was fairly uniform with no papular or rippled pattern as expected in macular amyloidosis and lichen amyloidosis. The differential diagnosis in our patient included lichen planus pigmentosus, drug-induced pigmentation, phototoxic contact dermatitis and melasma. The diagnosis of lichen planus pigmentosus was considered due to the patient being of Indian origin, distribution over the sun-exposed areas and the steady progression of the pigmentation. However, histological findings showed absence of basal vacuolar alteration affecting the epidermis. There was only focal basal vacuolar alteration around occasional hair follicles, in association with a mild perifollicular lichenoid infiltrate. Notably, areas of amyloid deposition were abundant in the papillary dermis and absent around hair follicles. Melanophages were mainly present in association with the amyloid deposits. Phototoxic contact dermatitis was also considered in view of the rapid onset of the pigmentation within a few hours of sun-exposure and the prolonged outdoor excursion on the day of development of rash. Against this diagnosis was the absence of a history of contact with topical photosensitising substances and there was no history of sunburn or discomfort preceding the rash. A drug-induced pigmentation was initially considered as she was on premarin which had been reported to cause photosensitivity in 4-6% of individuals and was capable of causing phototoxic reactions. Extensive variants of macular amyloidosis have been described: hyperpigmented, hypopigmented, poikilodermatous, biphasic, blaschkoid, linear,

nevroid, ichthyotic and diffuse generalised. The largest study on primary cutaneous amyloidosis to date is by Wang et al<sup>1</sup> in 2001 who retrospectively studied 794 patients with PLCA. PLCA was found to be quite common in Chinese patients. Amongst the many types of PLCA, lichen amyloidosis was the commonest. Amongst the macular amyloidosis cases, various variants were described including vitiliginous, biphasic and extensive diffuse types. In our patient the sun-exposure prior to the onset of the rash could be implicated. In a recent case report, sunlight was thought to be an important aggravating factor in the development of amyloidosis in some cases of PLCA.<sup>2</sup> As premarin (conjugated oestrogens) is known to be a photosensitiser and can cause a phototoxic reaction in 4-6% of individuals, we postulate that premarin may have contributed to the increase in photosensitivity in our patient who may have been susceptible to PLCA. Premarin has also been implicated in causing pigmentation in the oral mucosa in a 50-year old lady. A biopsy was performed and histology revealed focal melanosis.<sup>3</sup>

There has been some debate on the pathogenesis of PLCA. Chang et al<sup>4</sup> proposed that PLCA was a subgroup of interface dermatitis as they found dyskeratosis, vacuolar alteration of basal cells and pigmentary incontinence in their patients. The authors proposed that if a biopsy was taken at a late stage, only amyloid deposition and melanophages would be found perhaps offering an explanation as to why our patient showed basal vacuolar alteration and marked melanin incontinence.

Different mechanisms and two postulates, namely fibrillary body<sup>4</sup> and secretion theory<sup>5,6</sup> have been proposed on how amyloid is created but the mechanisms that cause epidermal damage and how amyloid fibrils are formed remains unknown. It has been hypothesised that focal epidermal damage possibly due to ultraviolet light, friction, etc. causes local degeneration of keratinocytes leading to apoptosis and conversion of

filamentous masses into amyloid material in the dermis. The current literature suggests that immune dysregulation present in PLCA prevents degenerating keratinocytes from being degraded.<sup>7</sup> The authors postulate that a subset of PLCA patients, especially those with extensive involvement, may have an associated immune disorder. The treatment of PLCA is disappointing.<sup>8</sup> Clinical improvement with dimethyl sulfoxide has been reported in anecdotal reports.<sup>9</sup> Das et al reported a case series of 36 patients with macular amyloidosis who responded to cyclophosphamide 50 mg daily for 6 months with marked reduction in itching and pigmentation.<sup>10</sup> Grimmer et al reported clearance in 2 patients with a combination of bath PUVA, photochemotherapy and oral acitretin at 0.5 mg/kg/day for 6 months.<sup>11</sup> A prospective left-right comparative study of UVB and PUVA versus potent topical steroids was performed on 20 consecutive patients with PLCA. The results showed that both the potent topical steroids and PUVA/UVB were effective and comparable in the treatment of amyloidosis.<sup>12</sup> In a recent side by side prospective trial comparing 532 nm and 1064 nm Q-switched Nd:YAG laser therapy in reducing the pigmentation induced by macular amyloidosis, results showed a net positive effect of both wavelengths but the 532 nm wavelength was found to be superior.<sup>13</sup> Another study by Hudson illustrated how UVB was found to be efficacious in the treatment of macular amyloidosis.<sup>14</sup>

In conclusion we report a case of PLCA that does not conform to previous reported cases in the literature. This case highlights that a skin biopsy is helpful in the diagnosis of unusual cases of dyschromia and the need for future research to study the possible role of sunlight as the inciting factor in macular amyloidosis.

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