Case Report

Familial Amyloidosis Cutis Dyschromica
- A Case Report and Review of the Literature

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Amyloidosis cutis dyschromica is a rare distinct type of primary cutaneous amyloidosis characterized by the presence of widespread hypopigmented as well as hyperpigmented macules. We herein report a 25-year-old male showing diffuse hyperpigmentation with hypopigmented spots over his whole body but sparing his face, hands and feet from the age of 8 years. His elder sister had also developed a similar skin pigmenrary defect since about the same age. Histopathology of the hyperpigmented lesion revealed increase of melanin in the basal layer, pigment incontinence and amorphous eosinophilic masses stained positive with Congo red in the papillary dermis. Amyloidosis cutis dyschromica was diagnosed. We report the familial case and the literature was reviewed. (Dermatol Sinica 26: 16-21, 2008)

Key words: Amyloidosis cutis dyschromica

INTRODUCTION

Primary cutaneous amyloidosis has a worldwide prevalence and is relatively commonly observed in Southeast Asian. It is a rare, chronic progressive skin disease which was defined as cutaneous amyloidosis in the absence of other systemic or dermatological disease. Amyloidosis cutis dyschromica is accepted as a specific type of primary cutaneous amyloidosis, first defined by Morishima in 1970. It is characterized by diffuse speckled hyperpigmentation with hypopigmented spots, mild or no itching, prepubertal onset, and small amounts of amyloid in the papillary dermis. We herein report a case of amyloidosis cutis dyschromica with family history and review the literature.

MATERIAL AND METHOD

A 25-year-old male has suffered from progressive and asymptomatic mottled hyperpigmentation involving almost the whole body present since 8 years old. The lesions appeared initially on his trunk. The hyperpigmentation had extended gradually over the years to involve his extremities. He also noticed spotty hypopigmentation among the hyperpigmented macules. He did not have photosensitivity or history of extensive sun exposure, inflammatory skin disease or systemic illness prior to the onset of the lesions. He was born to nonconsanguineous parents. The patient’s family tree was shown as follow (Fig. 1). His 26 year-old elder sister has more diffuse hyperpigmentation associated with spotted hypopigmentation almost on the whole body from the age of 8 years, and few concomitant clusters of pruritic papules with excoriation on both forearms and legs were also noted. She had received histopathological examination at a teaching hospital about 10 years ago, but no definite diagnosis was told.

Cutaneous examination revealed generalized mottled hyper- and hypopigmented varying-sized macules ranging from 2 to 13 mm involving almost the whole body (Fig. 2) in a symmetrical pattern which was more pronounced on trunk and bilateral lower legs with relatively sparing of the
Familial amyloidosis cutis dyschromica

A biopsy specimen taken from a pigmented macule on the non-sun-exposed buttock revealed amorphous eosinophilic material in the papillary dermis with an increase of melanin in the basal layer and pigment incontinence in the papillary dermis by haematoxylin & eosin stain. There were no alterations in the reticular dermis. The eosinophilic masses stained positive for Congo red (Fig. 3) and showed apple-green birefringence under polarized light indicating a deposit of amyloid substance (Fig. 4). Electron microscopy showed deposits of amyloid fibrils in the upper dermis surrounded by many collagen fibrils orientated in various directions (Fig. 5).

All other investigations (full blood count, biochemical profile, plasma protein electrophoresis, thyroid function test, ACTH, urine routine excretion) were within normal range.

Based on the clinical and pathological findings, the diagnosis of amyloidosis cutis dyschromica was made and the patient was scheduled for periodic follow-up.
Classically, the three major forms of primary cutaneous amyloidosis include lichenoid, macular and the rare nodular form. Macular amyloidosis is characterized by brownish patches with a confluent or rippled pattern, involving the upper back, arms and lower extremities. Lichen amyloidosis is the most common form and typically manifests as persistent pruritic hyperpigmented papules or plaques on the shins or other extensor surface of legs, forearms and upper back. Nodular amyloidosis presents as waxy nodules on the limbs, face, trunk or genitalia. Apart from the well-described forms of primary cutaneous amyloidosis, several atypical forms with diffuse involvement have been reported. These include poikiloderma-like amyloidosis, bullous, vitiliginous, anosacral forms and amyloidosis cutis dyschromica.

Amyloidosis cutis dyschromica, first described by Morishima in 1970, is an uncommon variant of primary cutaneous amyloidosis, which is characterized by the following features: (i) dotted, reticular hyperpigmentation with hypopigmented spots without papulation almost all over the body; (ii) no or little itchy sensation; (iii) onset before puberty; and (iv) small foci of amyloid closely under the epidermis.

In our case, although he and his elder sister both have concomitant pruritic papules on his bilateral forearms and on her both forearms and legs, other skin changes and histopathological findings meet the features of amyloidosis cutis dyschromica. Choonhakarn C et al. had reported six familial cases of amyloidosis cutis dyschromica, one of the 18 year-old male patient also had concomitant brownish lichenoid papules on the shins. The number of papular lesion was so few seems which did not affect the final diagnosis as other features showed the unique, non-pruritic, reticular hyperpigmentation with hypopigmented spots, generalized distribution, onset before puberty, amyloid deposits limited to the subepidermal region, and absence of other cutaneous and systemic involvements.

It is assumed to be a familial disorder with sun exposure as a major causal factor. Moriwaki et al. suggested that, although the pathogenesis of amyloidosis cutis dyschromica is unknown, genetic factors may lead to prolonged DNA repair in keratinocytes due to UV-C damage, and reduced repair of UV-B damage. The source of the amyloid material is controversial, and it has been suggested that repeated damage to the keratinocytes and then phagocytosis by histiocytes or fibroblasts producing amyloid materials in the skin. Amyloid deposits may initially be derived from cytkeratin, possibly following keratinocyte death. Keratinocyte destruction may occur as an initial result of apoptosis, which in turn leads to the amyloid formation.

Clinically, there are many diseases that are characterized by cutaneous dyschromia including amyloidosis cutis dyschromica, dyschromatosis universalis hereditaria, acropigmentation of Dohi (acral type of dyschromatosis universalis hereditaria), xeroderma pigmentosum, chronic radiodermatitis, malnutrition, topical application of chemicals (e.g., diphencyclopropenone or monobenzyl ether of hydroquinone), photooleukodermatitis (due to aloqualone, thiazides, or tetracyclines), acquired brachial cutaneous dyschromatosis, poikiloderma-like amyloidosis, and poikilodermatous syndromes.
pigmentosum and dyschromatosis universalis hereditaria do not show amyloid deposits in the skin. Poikiloderma-like amyloidosis is associated with light sensitivity, short stature and blister formation or palmoplantar hyperkeratosis. The clinical and pathological differences between some of these diseases are summarized in Table 1.

Various therapeutic modalities have been used in the treatment of cutaneous amyloidosis with variable success. Avoiding excess sun exposure and using sun protector is essential. Topical corticosteroids, keratolytics, dimethyl sulfoxide, capsaicin, and CO2 laser have all been tried with variable results. Systemic retinoids have been reported as effective. A Japanese case of amyloidosis cutis dyschromica has been treated with acitretin with a good response. However, our patient refused to take systemic retinoid, so we advised him to use broad-spectrum sunscreens.

In conclusion, clinically, when we see a patient with variation in the pigmentation of the skin, consisting of asymptomatic well-demarcated and irregular hyperpigmented macules admixed with various sized hypopigmented macules, amyloidosis cutis dyschromica must be considered in the differential diagnosis, and the histopathological confirmation should be made to reach a correct diagnosis. Family consultation for evaluating other family members is also important.

**REFERENCES**

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家族性色素異常性皮膚澱粉樣變性症
-病例報告及文獻回顧

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色素異常性皮膚澱粉樣變性症是原發性皮膚澱粉樣變性症的一個罕見而獨特的亞型，其特徵是在皮膚出現廣泛的色素沉著及色素脫失的斑點。我們在此報告一位25歲男性自八歲起在全身皮膚出現廣泛的色素沉著及色素脫失的斑點，病灶並未侵犯其臉部、手掌、及腳掌。他的姊妹亦於相近的年齡時在皮膚出現類似的色素異常。色素沉著的病灶其組織病理顯示在基底層有黑色素的增加，乳突狀真皮出現色素失調和均質的嗜伊紅性塊狀物質沈積，且以剛果紅染色呈陽性反應。配合臨床及病理發現診斷為色素異常性皮膚澱粉樣變性症。我們報告此一家族性病例並回顧相關文獻。(中華皮誌 26: 16-21, 2008)