

## Diffuse Pigmentation of Back and Arms: Macular Amyloidosis or Other?

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**Abstract-** The study was undertaken to answer the question that how many patients with pigmentation of back and arms actually have amyloid deposits in pathology. 44 patients presenting with diffuse pigmentation of back and arms (DPOBA) were selected. Skin biopsies were performed in all cases from the affected sites. On all formalin fixed and paraffin embedded specimens, the following histochemical stains were performed: Haematoxylin and eosin (H&E), Congo red and immunohistochemical staining using anti-cytokeratin monoclonal antibody. In 9 of 44 cases (20%), amyloid deposits were found. In the remaining 35 cases (80%), H&E, Congo red and immunohistochemical staining failed to show any amyloid deposition. We were unable to find amyloid deposition in most of the patients presented with DPOBA. It seems that the signs may be attributable other disorders with similar clinical but different pathophysiologic aspects.

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**Keywords:** Amyloid deposition; Anti-cytokeratin antibody; Macular amyloidosis; Pigmentation

### Introduction

In our daily practice, we regularly visit patients who complain about pigmentation on their skin, commonly on back and arms, in many cases associated with pruritus. Usually, the very unpleasant view and itching considerably decrease patients' quality of life. The most important differential diagnosis of this disorder is macular amyloidosis (MA) (1-3) while in most of the cases the skin biopsy does not show amyloid deposition (unpublished observation). This pigmentation may be a separate entity that we have termed here diffuse pigmentation of back and arms (DPOBA). We undertook the study to answer the question that how many patients with DPOBA actually have amyloid deposits. Accurate diagnosis should be work up in other studies with larger samples and more investigations.

Deposition of amyloid was searched by using haematoxylin and eosin (H&E), Congo red and immunohistochemical staining together to increase the sensitivity.

### Materials and Methods

This cross-sectional survey covered 44 Iranian patients during the year 2006. The study was granted ethical

approval by the Tehran University of Medical Sciences Ethics Committee and was supported by the university and health service grant.

Patients with diffuse hyperpigmentation of back, shoulders and arms and sometimes additional other sites of the body were enrolled. The patients were informed in detail and signed a written consent before entering the study. Detailed clinical history including history of systemic disease and results of physical examination were recorded in prepared questionnaires. Patients were asked about the habit of using coarse materials in clothes or in bathing staff to find the possibility of friction in long term. Patients' opinion about relation between the pigmentation and their emotional status and menstrual cycle was asked.

Three mm punch biopsies were performed in all cases from the affected sites (mostly back). All samples fixed in formalin and divided into three parts: one stained with H&E, one with Congo red and the last part underwent immunohistochemical staining using monoclonal anti-cytokeratin 5,6,8,18 antibody (Novocastra, UK). Two pathologists studied the samples separately to find amyloid substance.

A patient with both guttate hypopigmented and hyperpigmented lesions (mottled pigmentation) was biopsied from both sites. A total of 45 samples from 44

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patients were taken.

Using all three methods, the patients were classified into two groups: those who had amyloid deposits and those who did not. Samples considered positive if amyloid deposition was detected even by one of the three methods. According to the small number of amyloid positive group, any difference between the two groups may not have statistical significance.

## Results

In the study 41 patients (93%) were female and three patients (7%) were male. Amyloid depositions were found in nine patients (20%) including eight female and one male. The mean age of the patients in this study was 40.33 years in patients with positive amyloid test and 35.14 years in the rest. There was no history of systemic disease in patients except one patient in amyloid positive group and one in amyloid negative group who had hypothyroidism. Other characteristics of enrolled

patients are summarized in table 1.

H&E staining revealed amyloid deposits in nine samples out of 45 as an amorphous, eosinophilic, globular deposit in dermal papilla (Figure 1). One of these nine samples was weakly positive in Congo red staining while the others were negative. In these nine samples immunoreactivity with anti-keratin antibody was positive, and the amyloid deposits were observed as a brown material in upper dermis (Figure 2).

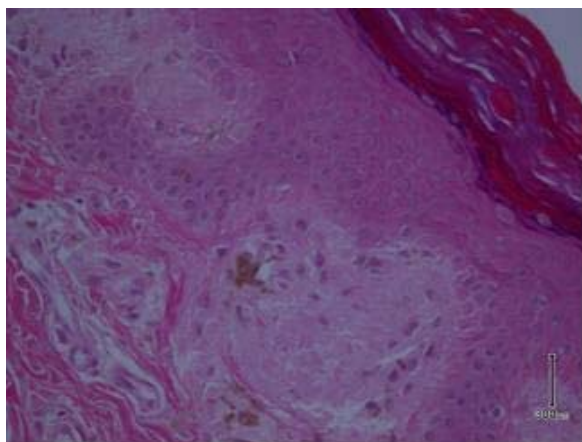
The remaining 36 samples (including the two biopsies taken from the patient with mottled pigmentation) did not demonstrate amyloid deposits in H&E, Congo red and immunohistochemical staining. In patients with negative amyloid staining, the pathologic findings were nonspecific as melanin deposition in upper dermis, mild papillary edema and sometimes periarterial infiltration by lymphocytes and histiocytes.

Table 2 shows some of the clinical findings and related factors in both groups.

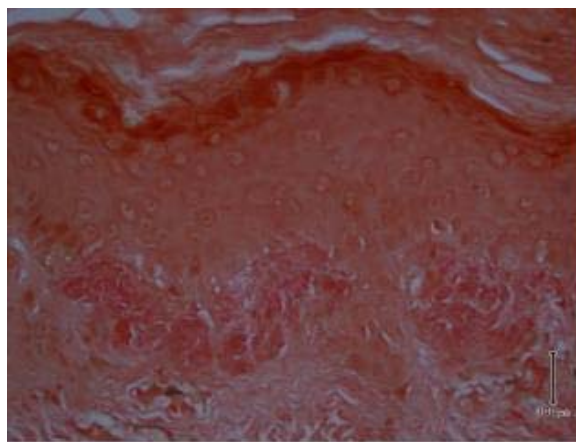
**Table 1.** Characteristics of the patients.

Amyloid Deposition n (%)	Mean Age (years)	Sex M/F	Skin Type (n) <sup>*</sup>	Positive Family History	Itching n (%)
Positive: 9 (20%)	40.33	1/8	III (1) IV (8)	0	8 (88%)
Negative: 35 (80%)	35.14	2/34	II (2) III (14) IV (16) V (3)	7	26 (72%)

\* According to Fitzpatrick classification



**Figure 1.** Histopathology view of macular amyloidosis (H&E).



**Figure 2.** Histopathology view of macular amyloidosis detected using anti-keratin antibody.

**Table 2.** Historic and clinical findings in the two groups of the study.

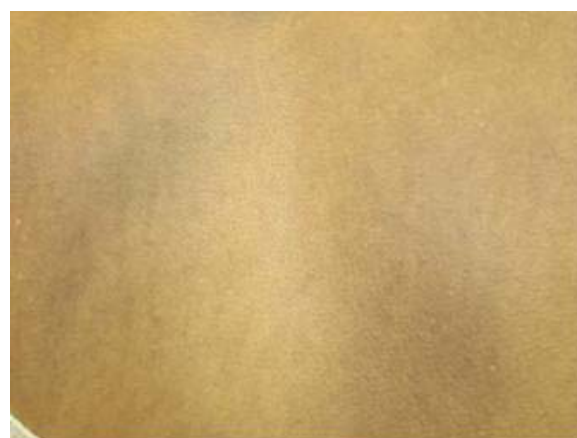
Amyloid Deposition	Shoulders, interscapular area, Upper arms	Other Sites	Associate d lichen amyloidosis (n)	Clinical features of the lesions n (%)	Suspicious Precipitating factors (nylon clothes, washcloth, brush) n (%)	Relation to emotional stress ‡	Relation to menstruation
Positive	9 (in all patients these 3 areas were affected)	7	2	Rippling Pig <sup>‡</sup> 7 (77%) Uniform Pig 1 (11.1%) Mottled Pig 1 (11.1%)	At least two 8 (88%)	Related 3 (33.3%)	Related 1 (20%)*
Negative	All patients had at least two affected	Chest (16) Lumbar (9)	0	Rippling Pig 13 (37.1%) Diffuse Pig 13 (37.1%) Mottled Pig (9/25%)	One factor 14 (40%) At least two 18 (51.4%) No factors 3(8.6%)	Related 14 (40%) Unrelated 13 (37.1%) Unknown 8 (22.8%)	Related 5 (16.6%)** Unrelated 23 (76.6%) Unknown 2 (6.6%)

†Pig: pigmentation

‡ According to the patient's point of view.

\* From 5 pre-menopausal women.

\*\* From 30 pre-menopausal women.

**Figure 3.** Pigmentation of back and arms: diffuse uniform pattern.**Figure 4.** Pigmentation of back and arms: patchy pattern.**Figure 5.** Pigmentation of back and arms: rippled pattern

## Discussion

In contrast to western countries, diffuse pigmentation of

back and arms is a common complaint among patients visiting dermatologists in our practice. Although this disorder may present as mottled, reticular or patchy

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configuration, the diffuse uniform pattern is more common (Figures 3-5). Different conditions may be responsible for this bizarre type of pigmentation such as macular amyloidosis, frictional melanosia, ashy dermatitis, dermatitis or lichen planus in post inflammatory stage. Amyloid deposition as MA is the first line suspect etiology. In clinical point of view, this disorder is not simply distinguishable from MA. Indeed they are the same in most of the times except when amyloidosis is associated with some lichenoid components (Figures 6 and 7). According to our experience, the skin biopsies do not show amyloid deposits in most cases. In this study, we were able to find amyloid deposition only in 20 percent of the patients. In our opinion; this pigmentation may be a separate entity that we have termed DPOBA because upper trunk, shoulders and arms are most common involved sites. On the other hand, DPOBA may be as an umbrella which encompasses a variety of different disorders or conditions with different etiology but similar clinical feature.

By searching the literature we noticed the studies that focused on clinically the same entity, considered MA (without pathologic confirmation) (1), frictional melanosia or towel melanosia, frictional amyloidosis or all as a same (2).

Here in this study, we discussed some factors as suspected ones in relation to the entity. One of these potential factors is gender of the patients. Even though, this disorder is seen in both sexes, female preponderance is notable (female to male ratio: 8 in amyloid positive and 17 in amyloid negative patients). Some studies have reported MA equally in men and women (3); however most of the previous studies have mentioned that the disease mostly involves females (1,4,5).



**Figure 6.** Macular amyloidosis with rippling and lichenoid component.



**Figure 7.** Macular amyloidosis with focus on rippled and lichenoid component.

This can be due to the fact that females call for help more than males, but may reflect a real difference.

Mechanical stress including friction with clothes may be another underlying factor (2). We found this history in both amyloid positive and amyloid negative patients with no statistically significant difference. So it is unclear if friction is a causative agent or only promotes a precipitated pathology.

Pruritus was a common finding in both groups. Although itching may reflect a running inflammatory process, its ability to induce friction should not be ignored.

History of atopy was another finding in our study. Again we found this factor to be of more prevalence in amyloid negative patients, with no statistical significance. One possible theory is dryness of the skin that promotes allergic pruritic reaction in such patients with consecutive friction and scratching that precipitate pigmentation.

Chemical materials used in clothes are among the other suspects. Some of them including poly-ethylene and synthetic nylon materials may have some effects on this disorder. Whether this finding is only a coincidence or shows a real relationship remains to be proved in further studies with larger sample sizes.

Another factor that can be considered is skin type or skin color of the patients. It is well-known that post lesional hyperpigmentation and pigmentary incontinence are more prevalent in people with higher skin types. In present study skin types of amyloid negative patients were higher than amyloid positive ones (Table 1). Although the relation between skin type and DPOBA has to be clarified, as a relative factor should be taken into account.

In conclusion, we could not find amyloid depositions

in 80% of the patients and it may be a clue for DPOBA to being a different entity. It is recommended to do more biopsies and use electron microscopy to detect little amounts of amyloid deposits. It is better to use frozen section and paraffin-embedded samples simultaneously for better detection of amyloid deposits.

It is also recommended to investigate more patients to find etiological factors. Considering more prevalence of the disorder in our society, by eliminating the risk factors, we may achieve effective solutions for this unpleasant, difficult-to-treat disease.

Positive immunoreactivity to anti-cytokeratin antibody (CK5,6,8,18) was detected in all 9 patients who had amyloid deposits in H&E staining. Cytokeratins are a family of intermediate filament proteins that are expressed in the epithelial cells (6). This finding can support the hypothesis that the amyloid deposit in MA is derived from filamentous degeneration of epidermal keratinocytes but how the substance is formed is still speculative (7-12). In normal skin, the degenerated cells dropped off into the papillary dermis are phagocytosed by macrophages, but in amyloidosis this removal mechanism may be slow or deficient due to unknown factors or overwhelmed by a massive deposition of keratin leading to amyloid formation (11).

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## References

1. Rasi A, Khatami A, Javaheri SM. Macular amyloidosis: an assessment of prevalence, sex, and age. *Int J Dermatol* 2004;43(12):898-9.
2. Siragusa M, Ferri R, Cavallari V, Schepis C. Friction melanosis, friction amyloidosis, macular amyloidosis, towel melanosis: many names for the same clinical entity. *Eur J Dermatol* 2001;11(6):545-8.
3. Sarkany R.P.E , Breathnach SM, Seymour C.A, et al. Metabolic and Nutritional Disorders. In: Burns T, Breathnach S, Cox N, et al. *Rook's Textbook of Dermatology*, 7<sup>th</sup> edition. Blackwell Scientific Publication. 2004;57:36-51.
4. Martin M. Black, Edward Upjohn, Sandra Albert. Amyloidosis. In: Jean L, Bologna, Joseph L, Jorizzo, Ronald P, Rapini. *Dermatology*. Mosby 2008: 623-631.
5. Taheri R. Prevalence of macular amyloidosis in north Iran. *Indian J Dermatol* 2007;52:192-3.
6. Cheung ST, Maheshwari MB, Tan CY. A comparative study of two Congo red stains for the detection of primary cutaneous amyloidosis. *J Am Acad Dermatol* 2006;55(2):363-4.
7. Eto H, Hashimoto K, Kobayashi H, Fukaya T, Matsumoto M, Sun TT. Differential staining of cytooid bodies and skin-limited amyloids with monoclonal anti-keratin antibodies. *Am J Pathol* 1984;116(3):473-8.
8. Yoneda K, Watanabe H, Yanagihara M, Mori S. Immunohistochemical staining properties of amyloids with anti-keratin antibodies using formalin-fixed, paraffin-embedded sections. *J Cutan Pathol* 1989;16(3):133-6.
9. Inoue K, Takahashi M, Hamamoto Y, Muto M, Ishihara T. An immunohistochemical study of cytokeratins in skin-limited amyloidosis. *Amyloid* 2000;7(4):259-65.
10. Masu S, Hosokawa M, Seiji M. Amyloid in localized cutaneous amyloidosis: immunofluorescence studies with anti-keratin antiserum especially concerning the difference between systemic and localized cutaneous amyloidosis. *Acta Derm Venereol* 1981;61(5):381-4.
11. Apaydin R, Gürbüz Y, Bayramgürler D, Müezzinoğlu B, Bilen N. Cytokeratin expression in lichen amyloidosus and macular amyloidosis. *J Eur Acad Dermatol Venereol* 2004;18(3):305-9.
12. Looi LM. Primary localized cutaneous amyloidosis in Malaysians. *Australas J Dermatol* 1991;32(1):39-4.