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# To study the correlation of clinical, dermoscopic and histopathological features of clinically suspected macular amyloidosis

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## Abstract

**Background:** Macular amyloidosis is a common acquired hyperpigmented disorder seen predominantly in women involving the extremities and upper back which is cosmetically displeasing and may amount to emotional stress. It clinically presents as ill-defined hyperpigmented macules which gradually coalesce to form symmetric patches with characteristic rippled pattern.

**Objectives:** To study the correlation of clinical, dermoscopic and histopathological features in patients with clinically suspected macular amyloidosis.

**Materials & Methods:** A total of 50 patients with clinically suspected macular amyloidosis were enrolled in this cross-sectional study. A detailed history, cutaneous examination and dermoscopic patterns were documented. A punch biopsy was taken from the site where dermoscopic examination was done and stained with a) Hematoxylin & Eosin examined under light microscope b) Congo red stain observed under polarized microscope for amyloid deposits.

**Results:** Out of 50 patients with clinically suspected macular amyloidosis, 41 were females and 9 were males with male to female ratio being 1:4.5. The age ranged between 20 to 49 years with mean age of 27.64 years. Pumice stone (42%) was the most common abrasive material used for bathing. Hyperpigmentation in rippled pattern (72%) was the commonest morphological pattern seen. Extensor aspect of the upper limbs and upper back (46%) were the commonest sites of involvement. On dermoscopy, majority revealed a central brown hub (38%)/ white hub (18%) with surrounding radiating streaks of pigmentation. Majority of patients (76%) on histopathological examination showed amyloid deposits which with Congo red stain showed apple-green birefringence under polarized microscope.

**Conclusion:** The correlation between clinical, dermoscopic and histopathological features was statistically significant ($p<0.001$). Both the sensitivity and specificity of diagnosis of macular amyloidosis with the use of dermoscopy in our study was 100%.

**Keywords:** Clinically suspected macular amyloidosis; Rippled pattern; Central brown hub/ white hub; Amyloid deposits; Apple green birefringence.

## Introduction

Amyloidosis is a spectrum of diseases characterized by extracellular deposition of amyloid and is usually associated with considerable tissue dysfunction. Macular amyloidosis (MA) is a major subtype of primary localized cutaneous amyloidosis.[1] It is a common acquired hyperpigmented disorder seen predominantly in young women involving extremities, upper back and frictional sites which can be cosmetically displeasing and may amount to emotional stress.

The exact etiology of macular amyloidosis is not known. Risk factors such as race (Asian), sex (female), genetic factors, sun exposure, friction and atopy have been suggested. Two theories, namely fibrillar body theory and secretory theory have been proposed for the deposition of amyloid protein in the skin though they are not conclusive.[2,3] Macular amyloidosis manifests clinically as greyish brown macules which coalesce to form symmetric hyperpigmented patches having a characteristic reticulate or rippled pattern most frequently distributed over the upper back, extensor aspect of arms, forearms and legs and less frequently over the chest and thighs.[4-6] It needs to be differentiated from other acquired hyperpigmented disorders like ashy dermatosis, post inflammatory hyperpigmentation, resolving lichen planus, lichen planus pigmentosus, Berloque dermatitis and Riehl's melanosis.[7]

Histopathological examination with Hematoxylin and Eosin (H&E) staining reveals amorphous eosinophilic masses of amyloid in the upper dermis though small deposits of amyloid can be missed under routine examination.[3,8] Congo red staining is a commonly used specific stain in confirmation of amyloidosis wherein amyloid appears pink and produces apple green birefringence under polarized microscopy.[9,10] Of late, Dermoscopy is proving to be an invaluable non-invasive tool in diagnosis of pigmented skin lesions. There is a paucity of studies on dermoscopic findings in macular amyloidosis and a single study revealed multiple uniform small brown central hubs with brown fine streaks radiating from the centre.[8]

Most of the cases with hyperpigmented patch on the back and extremities are usually diagnosed as macular amyloidosis and it is also been known as frictional melanosis, peculiar melanosis, nylon friction dermatitis and recently as frictional amyloidosis despite the absence of amyloid deposition in majority of these

cases.[11,12] As a result the treatment of these cases have been often disappointing. Since the exact etiology of macular amyloidosis is not known, a complete history and histopathological examination will help us give an insight to the disease. The role of dermoscopy in macular amyloidosis is yet to be explored with very few studies available in world literature. Any hyperpigmentation, on exposed or unexposed parts of body is a cosmetic concern and there are no Indian studies on correlation of clinical, histopathological & dermoscopic features of MA which makes it prudent to study this topic.

## Material and Methods

Fifty patients with clinically suspected MA were enrolled on an out-patient basis attending the Department of Dermatology, Venereology and Leprosy, Adichunchanagiri Hospital and Research Centre, B.G. Nagara. This was a cross-sectional study done from Dec 2014 – May 2016. Patients more than18 years of age with clinically suspected macular amyloidosis were enrolled in the study. Patients less than18 years of age, pregnant and lactating women, previous history of treatment with topical medication and history of associated systemic disorders/ drug intake leading to cutaneous hyperpigmentation were excluded from the study. A written informed consent was taken from all the patients after approval from the Institute's Ethical Committee. A detailed history was taken as per the prepared questionnaire with emphasis on age of onset, distribution, usage of frictional objects, associated symptoms and family history. A thorough clinical examination was done with emphasis on pattern, distribution, symmetry and skin changes around MA. The lesions were then examined with the aid of a videodermoscope and the color and pattern of examined lesions were documented. Five millimeter punch biopsies were performed in all cases from the corresponding site where dermoscopic examination was done. All the slides were then stained for demonstration of amyloid deposits with: a) Hematoxylin and Eosin (H&E) and examined under light microscope b) Congo red stain and observed under polarized microscope.

## Results

This study was conducted in the Department of Dermatology, Venereology and Leprosy, Adichunchanagiri Hospital and Research Centre, B.G. Nagara, for a period of 18 months wherein 50 patients with clinically suspected macular amyloidosis were recruited. Majority of patients (68%) were in the age group of 20-29 years. The mean age of patients with clinically suspected macular amyloidosis was 27.64 years. Females (82%) outnumbered males (18%) with male to female ratio being 1:4.5. Majority of patients with clinically suspected macular amyloidosis were students (54%) followed by housewives (34%). Majority of the patients (88%) gave history of insidious onset. Only 5 patients (10%) gave positive family history. History of friction (68%) was found to be the most common aggravating factor wherein usage of pumice stone for bathing (42%) was the most common abrasive material followed by nylon brush (26%). Majority of patients (54%) had a Fitzpatrick's skin type IV followed by skin types III (44%). The predominant morphological pattern seen was hyperpigmentation in rippled pattern (72%). The most common site of involvement was extensor aspect of arms, forearms and upper back (46%) in our study (Fig. 1 & 2). All the patients (100%) with clinically suspected macular amyloidosis had a bilateral distribution. Thirty eight (76%) out of fifty patients showed dermoscopic findings consistent with macular amyloidosis, the most common being a central brown hub (38%)/ white hub (18%) with radiating streaks of pigmentation and a central brown hub with leaf like projections of pigmentation (20%). Twelve patients (24%) showed non-specific findings on dermoscopy (Fig. 3 & 4). On histopathological examination, basket-weave orthokeratosis with pigmentation of basal cells (44%) in the epidermis was the commonest feature seen followed by pigmentation of basal cells (20%), hyperkeratosis with pigmentation of basal cells (18%) and normal epidermis (18%) in the subjects (Fig. 5). Thirty eight (76%) out of fifty patients with clinically suspected macular amyloidosis showed amyloid positive and pigment incontinence on histopathological examination (HPE) which under polarized microscopy showed apple green birefringence with Congo red stain (Fig. 6, 7A & B). In our study, the correlation between clinical and dermoscopic findings was statistically significant ($p<0.001$). The correlation between clinical findings and histopathological features was statistically significant ($p<0.001$). The correlation between dermoscopic findings with histopathological features was statistically significant ($p<0.001$). In our study, there was a statistically significant correlation between clinical, dermoscopic and histopathological findings ($p<0.001$). The sensitivity and the specificity for diagnosis of MA were found to be 100% with the use of dermoscopy in this study.

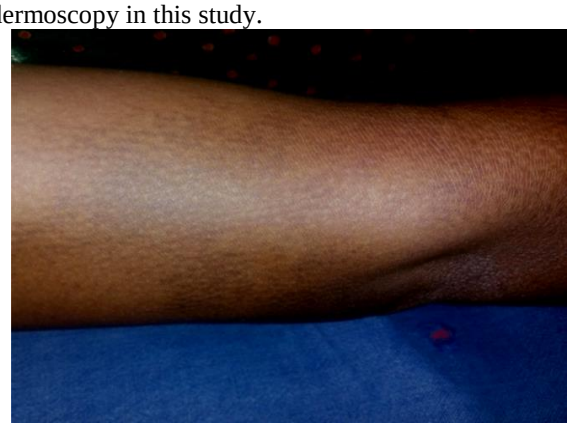

**Fig. 1: Hyperpigmentation in rippled pattern over the extensor aspect of arm**

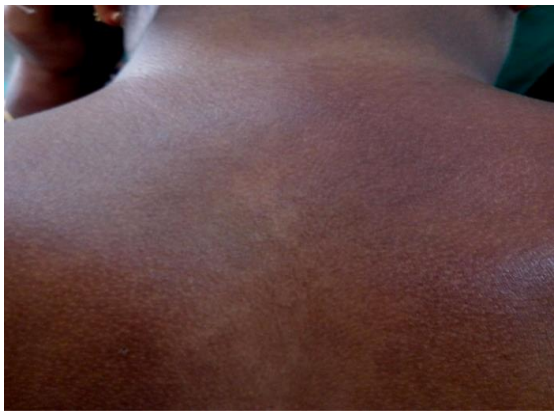

**Fig. 2: Hyperpigmentation in rippled pattern over the upper back**

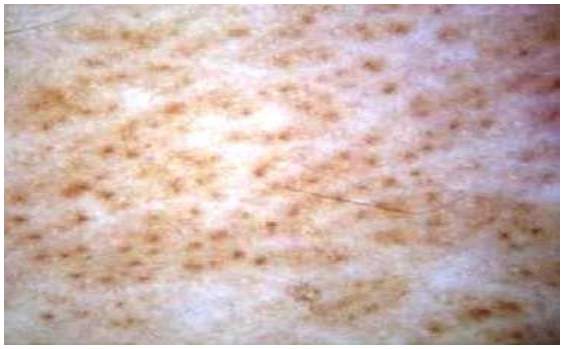

**Fig. 3: Central hyperpigmented (brown) hub with peripheral streaks of pigmentation on dermoscopy**

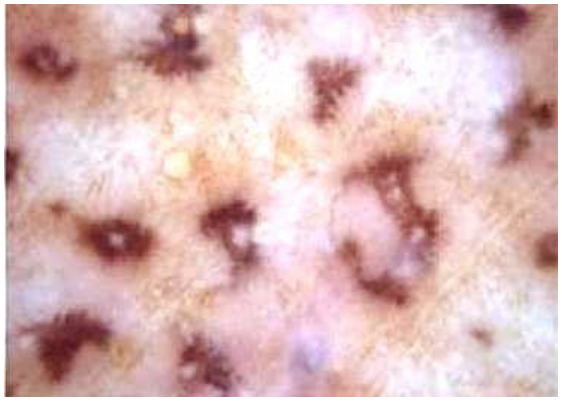

**Fig. 4: Central hypopigmented (white) hub with peripheral streaks of pigmentation on dermoscopy**

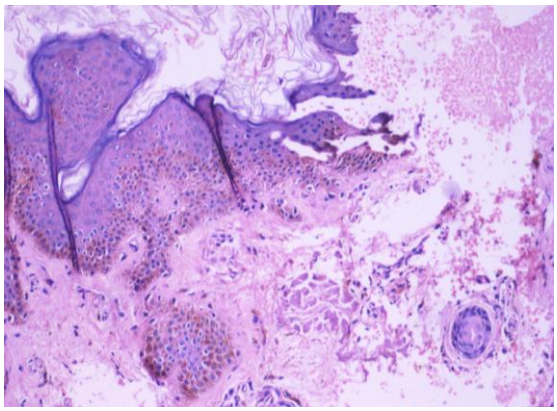

**Fig. 5: Basket weave orthokeratosis and basal cell pigmentation in the epidermis, amorphous amyloid deposits and pigment incontinence in the papillary dermis (H & E 40X)**

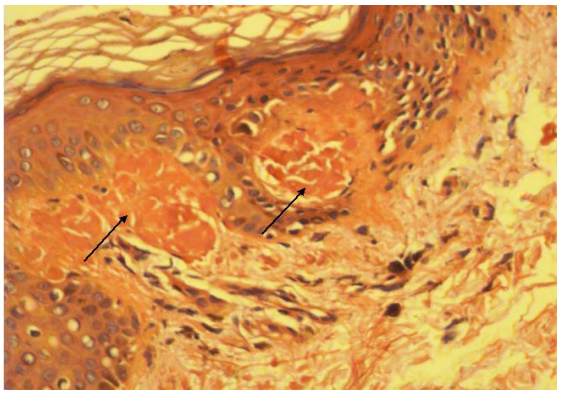

**Fig. 6: Amyloid deposits seen in orange red color (black arrow) in the papillary dermis (Congo red 40X)**

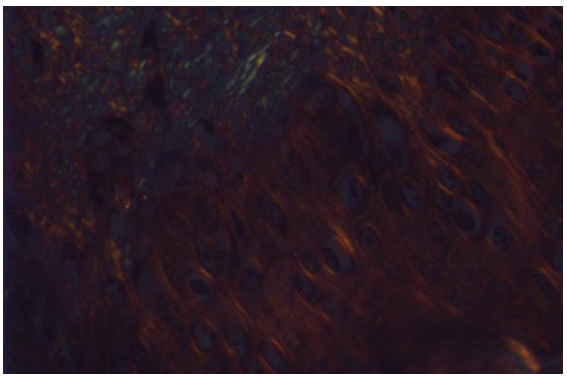

**Fig. 7a**

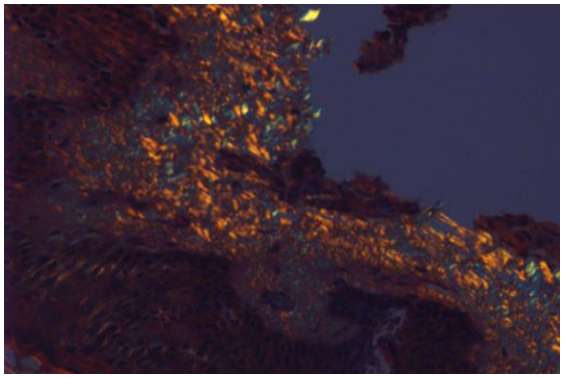

**Fig. 7b**

**Fig. 7 A & B: Shows apple green birefringence of the amyloid deposits under polarized microscope (Congo red)**

## Discussion

Macular amyloidosis has been described as a disease presenting with pigmented macules in a characteristic rippled pattern over the extensor aspect of arms, forearms and the interscapular area.[1,13] This condition is particularly common in Asians.[14]

In the present study, majority (68.0%) of the patients with clinically suspected MA were between 20-29 years. In the current study relatively younger population were involved more, when compared to studies done by Jampani K et al[15] (31-50 years) and Jayabhanu AA et al[14] (41-50 years).

In the present study, females outnumbered males (male: female = 1:4.5) which is comparable with studies done by Al-Helalat M et al[1] (1:7), Bandhlish A et al[3] (1:7.3) and Rasi A et al[17] (1:9).

Out of the 50 patients with clinically suspected macular amyloidosis, majority of the patients 27 (54%) were students followed by housewives 17 (34%). In contrary, study done by Jampani K et al[15] wherein majority were housewives (54.54%) followed by farmers (36.36%).

In our study, majority of patients (88%) had insidious onset. Results could not be compared due to paucity of similar studies.

In our study, only 1 (2%) patient had itching as an associated symptom. In contrary, study done by Jampani K et al[15] wherein 63.63% patients of MA had itching. Similarly, Bandhlish A et al[3] reported that half the patients (50%) experienced pruritus of varying degrees and three patients experienced severe pruritus.

In the current study, friction as an associated predisposing factor was found in 34 (68%) of the patients wherein majority (42%) gave history of using pumice stone as an abrasive material for bathing which is consistent with studies done by Jampani K et al[15] (Plastic brush and coir), Razvi F et al[16] (Nylon brush), Jayabhanu AA et al[14] (Vegetable fiber), Taheri R et al[6] (Nylon towels). In contrast, studies done by Rasi et al,[17] Somani VK et al[18] and Bandhlish A et al,[3] they found that the role of friction in macular amyloidosis to be inconclusive.

In the present study, family history was present in 10% of the patients with clinically suspected MA, our observation was similar to a study done by Taheri R et al.[6]

In our study, a majority (54%) belonged to the skin type IV which was consistent with a study done by Ghodsi SZ et al.[11] In contrary, Bandhlish A et al[3] reported that 39 (78%) out of 50 patients screened in their study belonged to skin phototype III.

Majority of patients with clinically suspected MA, the predominant site was the upper back, extensor aspect of arms & forearms (46%) which is comparable with study done by Bandhlish A et al.[3] However, Razvi F et al[16] in their study reported shin to be the commonest site of involvement in addition. In the present study, all the patients had bilateral symmetrical distribution. Hyperpigmentation in rippled pattern was noted in majority (72%) of the patients which is consistent with studies done by Bandhlish et al,[3] Jampani K et al,[15] Jayabhanu AA et al,[14] Ghodsi SZ et al[11] and Krishna A et al.[4] However, in a study done by Razvi F et al[16] they reported that diffuse pigmentation was the commonest presentation.

In the present study, majority (58%) showed a central brown hub with surrounding radiating streaks of pigmentation and leaf like projections of pigmentation. A central white hub with surrounding radiating streaks of pigmentation was seen in 9 (18%) of the subjects. Non-specific features were found in 12 (24%) of the subjects. In study done by Chuang YY et al[8] they have reported that all 18 cases shared a common dermoscopic pattern characteristic of MA which was a central hub, which could be either white or brown, surrounded by various configurations of pigmentation such as fine streaks, leaf like extensions or a noncircular thick pedal projection with a smooth border which was similar to the present study. There were no similar studies in Indian population to compare our results.

In the current study, histopathological assessment of epidermis revealed that basket-weave orthokeratosis & pigmentation of basal cells was the most common finding seen (44%) followed by pigmentation of basal cells (20%). However, in a study done by Bandhlish A et al[3] and Jayabhanu AA et al[14] on histopathological assessment showed normal epidermis. In a study done by Jampani K et al[15] they revealed that pigmentation of basal cells, hyperkeratosis & acanthosis were the commonest findings.

In the present study, majority (76%) showed amyloid deposits in papillary dermis & pigment incontinence under light microscopy and apple green birefringence with Congo red staining under polarized microscopy. Our observation was similar to studies done by Vijaya B et al,[10] Kudur MH et al,[5] Jayabhanu AA et al[14] and Bandhlish A et al.[3]

In the present study, majority of patients (72%) presented with hyperpigmentation in rippled pattern correlating with characteristic dermoscopic findings which was statistically significant (p<0. 001). Results could not be compared due to paucity of similar studies.

In the present study, out of 50 clinically suspected MA patients, majority of them (72%) presented with a common morphology of hyperpigmentation in rippled pattern on histopathology were positive for amyloid deposits and showed apple green birefringence with Congo red stain under polarized microscopy and the correlation was statistically significant (p<0. 001).

Out of 50, majority (76%) of patients with clinically suspected MA showed characteristic dermoscopic features (central brown/white hub with radiating streaks of pigmentation) and on histopathology were positive for amyloid deposits which on Congo red stain showed apple green birefringence under polarized microscopy. Hence, the correlation of dermoscopic and histopathological examination was statistically significant (p<0. 001).

In a similar study done by Chuang YY et al they found an association between dermoscopic and histopathological findings which were, brown pigmentation under dermoscopy correlated with basal hyperpigmentation, pigment incontinence and melanin granules with amyloid deposits in the papillary dermis. The brown central hub correlated to loose basket-weave orthokeratosis and the white hub to marked hyperkeratosis histopathologically.[8]

Out of 50 clinically suspected MA patients, 36 presented with hyperpigmentation in rippled pattern which correlated with characteristic dermoscopic findings consistent with MA and amyloid deposits in dermis histopathologically. The clinical, dermoscopic and histopathological correlation of 50 clinically suspected MA patients in our study was statistically significant (p<0. 001).

## Conclusion

The predominant morphological pattern seen was hyperpigmentation in rippled pattern over the upper back, extensor aspect of arms and forearms, on dermoscopic examination revealed characteristic central brown hub (38%)/ white hub (18%) with radiating streaks of pigmentation and on histopathological examination showed amyloid deposits in the papillary dermis which on Congo red stain showed apple green birefringence under polarized microscope. The clinical, dermoscopic and histopathological correlation of 50 clinically suspected MA patients in our study was statistically significant (p<0. 001).

Macular amyloidosis is a potentially disfiguring disorder with its different clinical appearances. Since it is very difficult to diagnose cases on the basis of naked eye examination alone, a non-invasive, diagnostic tool like a ‘dermatoscope’ which provides better magnification can be used in day to day practice. In the modern day world, dermatologists can adapt to usage of a small, handy diagnostic tool with a better magnification than a simple hand lens.

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