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Research Article

Clinicoepidemiological and histopathological study of cutaneous amyloidosis with histopathological correlation

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ABSTRACT

Background: Primary localized cutaneous amyloidosis is a commonly encountered problem in our scenario. As there is paucity of Indian studies on this subject, a clinico-epidemiological study was carried out. Objectives of the study were to make an insight into the common clinical variants of primary localized cutaneous amyloidosis, to compare the age and sex distribution of various forms of PLCA, to study the etiological factors involved in primary localized cutaneous amyloidosis and to study the incidence, association, distribution, and histological correlation of PLCA.
Methods: Patients having features of primary localized cutaneous amyloidosis attending the outpatient Department of Dermatology, Image Hospitals Hyderabad, India from June 2009 to 2010 was be enrolled into the study. Collection of data by history taking, clinical examination and skin biopsy was done in selected cases.
Results: Positive family history was noted in a considerable number of patients. Pigmented macules with rippled pattern in macular amyloidosis and pigmented hyperkeratotic papules in lichen amyloidosis are the most common presentations and a combination of macular and lichen amyloidosis is seen in biphasic amyloidosis. Site most commonly involved in macular amyloidosis is extensor aspect of arm and anterior aspect of lower leg in lichen amyloidosis.
Conclusions: Nodular cutaneous amyloidosis and sometimes lichen amyloidosis are associated with systemic amyloidosis. So such patents likely to develop systemic amyloidosis should be screen internally to rule out systemic amyloidosis.

Keywords: Primary localized cutaneous amyloidosis, Macular amyloidosis, Lichen amyloidosis, Biphasic amyloidosis

INTRODUCTION

Amyloidosis refers to abnormal extracellular tissue deposition of one of the family of biochemically unrelated proteins that share certain characteristic staining properties, including apple green birefringence of Congo red stained preparations viewed under polarized light and fibrillar ultra-structure.[1] Amyloid deposition may occur throughout many organs of the body (Systemic Amyloidosis) or may be restricted to a single tissue site (Organ –Limited / Localised Amyloidosis).[1]

Systemic amyloidosis is further classified into primary systemic amyloidosis, secondary systemic (reactive systemic) amyloidosis and heredo familial amyloidosis.

Localized/organ-limited amyloidosis can be classified into cutaneous amyloidosis, endocrine and cerebral amyloidosis. Cutaneous amyloidosis can be classified as Primary Localised cutaneous amyloidosis and Secondary cutaneous amyloidosis i.e secondary to systemic amyloidosis.[2] Primary localised cutaneous amyloidosis (PLCA) refers to deposition of amyloid in apparently

normal skin with no evidence of deposits in internal organs.[2] PCLA can be classified into three principle categories:

- Macular amyloidosis
- Lichen (papular) amyloidosis
- Nodular (tumefactive) amyloidosis

Macular amyloidosis is characterised by dark brown pigmentation in rippled pattern mainly over the upper back, arms and forearms. Lichen amyloidosis presents as persistent pruritic papular lesions predominantly over lower limbs. Macular forms are more common in India, Middle East, Central and South America and Lichen forms are more common among Chinese individuals.[3]

Nodular amyloidosis, a rare type of Primary Cutaneous Amyloidosis characterized by one or several nodules of 1-3 cm, presents usually on legs or face. Poikiloderma like cutaneous amyloidosis, bullous amyloidosis, vitiliginous amyloidosis and anosacral amyloidosis have been reported occasionally. The term Biphasic amyloidosis was proposed by Brownstein et al to describe patients with mixed macular and papular lesions.[4]

Etiopathogenesis of cutaneous amyloidosis is poorly understood. PCLA appears to be multifactorial in origin, however environmental and genetic factor appears to play an important role in its pathogenesis. The proposed mechanisms for keratinocyte degeneration are chronic friction induced by nylon bath sponges, pumice stones and coconut fibres.[5] Histopathology of papular and macular forms of PLCA shows amyloid deposits confined to papillary dermis, while in nodular forms – dermis, subcutis and blood vessel walls are diffusely infiltrated with amyloid.

Special stains used to detect amyloid proteins are congo red, pagoda red, thioflavin- T, crystal violet, methyl violet and toluidine blue. Electron microscopic examination is of importance in establishing firm diagnosis. Most cases of cutaneous amyloidosis remain chronic and refractory to treatment. Topical glucocorticoids, intra-lesional steroids, dermabrasion and topical retinoid have been used with varied success.

METHODS

Study was conducted on outpatient department of dermatology and Venereology at Image hospitals Ameerpet, Hyderabad, India from January 2009 to January 2010.

Type of study and consent

It is an open label non interventional cross sectional study Ethical and scientific committee of Image Hospitals consent has been taken. Benefits of the study purpose explained to the patient and their consent taken.

Inclusion criteria

- New patients of all age groups and box sexes with a clinical diagnosis of cutaneous amyloidosis
- Patients with all clinical types of cutaneous amyloidosis, Macular amyloidosis, Lichen amyloidosis, biphasic amyloidosis

Exclusion criteria

- Pregnant women were excluded from the study.
- Patients with systemic amyloidosis were excluded from the study
- Old patients of cutaneous amyloidosis on follow up were excluded from the study i.e. those on treatment cutaneous amyloidosis were excluded from the study

Study population

A Prospective study was conducted over a period of one year with 50 new untreated patients with clinical diagnosis of Cutaneous Amyloidosis. They were all consecutive patients who were regularly coming to the outpatient department of Dermatology at Image hospital, Ameerpet Hyderabad, India.

Detailed examination with regard to hypertension diabetes, epilepsy, respiratory diseases, back ache, atopy and other medical problems was taken. Through general and systemic examination was carried out to rule out any systemic problems (diabetis, hypertension, TB, atopy). Each patient was subjected to a detailed history and examination details were noted with regard to duration, onset progression, provoking factors, photo exposure, associated cutaneous and systemic disease, family history, distribution, past similar complain, any medication (systemic and topical).

After detailed history taking, through general and physical examination was done to look for any other associated abnormality, systemic examination to rule out systemic abnormality, cutaneous examination done with respective morphology, distribution, site, type of lesion, secondary changes all the findings noted and patients was further investigated as follows.

Data collection

Routine investigation was done in all cases like Hb, TLC, DLC, Pt count urine examination for sugar, Albumin, microscopy RFT, RBS, LFT, Thyroid Profile and ultra sound Abdomen to rule out Liver involvement. All 50 patients were recalled and skin biopsy for routine Histopathology was done. The slide studied in detail to know the histopathology features and different clinical types. Special staining of amyloid with alkaline Congo red was done. Electron Microscopy was used to confirm the deposition of Amyloid.

Data analysis

Statistical Analysis was done using P-Value using variable SD Mean. Ch-square Test was done to decrease the discrepancy between different variables.

RESULTS

Out of 50 patients of cutaneous amyloidosis, 37 patients were of macular amyloidosis (74%), 9 patients were lichen amyloidosis (18%) and biphasic amyloidosis was seen in 4 patients (Table 1).

Table 1: Distribution of cases according to clinical types.

Clinical type	Number	Percentage
Macular amyloidosis	37	74
Lichen amyloidosis	09	18
Biphasic amyloidosis	04	08
Total	50	100

Out of 50 patients with cutaneous amyloidosis, 32% were asymptomatic and 68% were symptomatic. In macular amyloidosis, 17 patients (45.9%) were asymptomatic. In both lichen and biphasic forms all the patients (100%) were symptomatic (Itching) (Table 2).

Pigmented macules with rippled pattern were seen in all cases of macular amyloidosis. Pigmented hyperkeratotic papules were seen in all cases of lichen amyloidosis and biphasic amyloidosis (Table 3).

Table 2: Distribution of cases according to symptoms.

	Macular amyloidosis		Lichen amyloidosis		Biphasic amyloidosis	
	Number	Percentage	Number	Percentage	Number	Percentage
Asymptomatic	17	45.9	00	00	00	00
Symptomatic	20	54.1	09	100	04	100

Table 3: Morphology of lesions.

	Macular amyloidosis		Lichen amyloidosis		Biphasic amyloidosis	
	Number	Percentage	Number	Percentage	Number	Percentage
Pigmentation	37	100	09	100	04	100
Macules with rippled pattern	37	100	00	00	04	100
Hyperkeratotic papules	00	00	09	100	04	100
Lichenification	03	8.1	08	86.6	02	50

Table 4: Distribution of cases according to associated conditions.

Systemic disease	Macular amyloidosis	Lichen amyloidosis	Biphasic amyloidosis
Systemic amyloidosis	00	00	00
Diabetes	01	00	00
Hypertension	02	04	00
Hypothyroidism	00	00	00
Atopy	00	00	00

No association with any illness was found in patients with biphasic amyloidosis. 4 patients (13.33%) of lichen amyloidosis and 2 (3.8%) patients of macular amyloidosis had hypertension and 1 patient of macular amyloidosis had Diabetes Mellitus no patient was associated with hypothyroidism and atopy in the present study of 50 patients Cutaneous amyloidosis 37 were macular amyloidosis, 9 were lichen amyloidosis and 4 were biphasic amyloidosis (Table 4). In our study the entire 50 patient recalled and were biopsied and

histopathology was studied with reference to hyperkeratosis, hypergranulosis, irregular acanthosis, and other less important features like basal cell liquefaction, melanin incontinence, and necrotic keratinocytes, irregular acanthosis was seen in 17 patients.

Table 5: Distribution as per type of amyloidosis.

Type of amyloidosis	No. of biopsies	Amyloid deposition in papillary
Macular amyloidosis	37	37
Lichen amyloidosis	09	09
Biphasic amyloidosis	04	04

Table 6: Distribution as per histopathological findings.

Histopathological findings	Macular amyloidosis		Lichen amyloidosis		Biphasic amyloidosis	
	Present	Absent	Present	Absent	Present	Absent
Irregular acanthosis	05	32	08	01	04	00
Hypergranulosis	00	37	08	01	04	00
Hyperkeratosis	00	37	08	01	04	00
Elongation of reteridge	03	32	08	01	04	00
Papilolomatosis	00	37	03	06	03	01
Inflammatory infiltrates	35	02	07	02	04	00
Melanin incontinence	33	04	09	00	04	00
Necrotic keratinocytes	32	05	03	06	04	00

Hypergranulosis was seen in 12 patients, hyperkeratosis was seen in 12 patients, thining and elongation of reteridges was seen in 15 patients, papillomatosis was seen in 6 patients, inflammatory infilterate was seen in 46 patients, pigmentary incontinence was seen in 46 patients, necrotic keratinocytes was seen in 39 patients. While basal cell liquefactive degeneration was seen in non of the patients. So the commonest finding seen were dermal changes i,e inflammatory infilterate seen in macular amyloidosis followed by lichen and biphasic amyloidosis. Biphasic amyloidosis had both epidermal and dermal changes while lichen amyloidosis had mainly epidermal changes.

DISCUSSION

During course of 1 year prospective study there were 50 new patients with a diagnosis of cutaneous amyloidosis among 4468 new patients who attended the skin OPD. So the incidence of cutaneous amyloidosis was 1.13% among the patients attending skin OPD.

In this study, out of 50 cases of cutaneous amyloidosis, 37 (74%) were of macular amyloidosis, 9 (18%) were of lichen amyloidosis and 4(8%) were of biphasic amyloidosis. Al-Ratrout JT et al reported that 90% of the cases were macular amyloidosis while only 10% were lichen amyloidosis.[6] Kibbi AB et al found macular amyloidosis in 74.13% of the patient and lichen amyloidosis in 25.86%.[7] Looi LM observed that only 26% were macular amyloidosis while 74% were lichen amyloidosis.[8]

In the present study, cutaneous amyloidosis was more common in the age group of 21-30 years (48%), Macular amyloidosis was more common in the age group of 21-30 years (40.5%), Lichen amyloidosis was most frequently seen in the age group of 31-40 years (77.7%), Biphasic amyloidosis was most frequently seen in the age group of 41-50 years (75%). Al-Ratrout JT et al found that cutaneous amyloidosis was commonest in the age group of 31-40 years (28.57%), macular amyloidosis was common in the age group of 31-40 years (30%), lichen amyloidosis in the age group of 31-40 years, 41-50 years with 27.27% each.[6] Ozkaya-Bayazit et al observed that majority of the patients of cutaneous amyloidosis belonged to the age group 41-50 years (38.46%), Macular amyloidosis was seen mostly in the age group of 41-50 years (40%).[9]

In the present study of 50 patients of cutaneous amyloidosis, 17 were males (34%) and 33 (66%) were females, with a male to female ratio was 1: 2. Ozakaya-Bayazit E et al observed that 15.38% were males and 84.62% were females with a male to female ratio of 1:5.5.[9] Black MM et al observed that 61.9% were males and 38.1% were females. Male to female ratio was 1.63:1.[10] Taheri R studied 100 cases of macular amyloidosis, 85 patients were females and 15 were males, female: male ratio was 9:1.[11]

Majority of the patients with cutaneous amyloidosis had duration between 6 months to 1 year (36%). Duration of 2-5 years was seen in 32% of the patients, 20% had duration more than 5 yrs and duration less than 6 months

was seen in 12%. In the present study shortest duration of cutaneous amyloidosis is 2 months and longest duration is 8 years. Sailm T et al reported duration between 6 months to 20 months.[12] Tay CH et al found 2.5% with less than 1 year duration. Duration of 5-10 years and 10-20 years were seen in 22.5% each. Duration of 20-40 years was seen in 25% while 27.5% had duration of 1-5 years. The shortest duration was 3 months and longest was 40 years with an average of 10 years and 3 months.[13]

Out of 50 patients with cutaneous amyloidosis, 32% were asymptomatic and 68% were symptomatic. In macular amyloidosis 22 patients out of 37 (54.1%) were symptomatic. In both papular and macular forms all the patients (100%) were symptomatic. Salim T et al reported that 90% of the patients with lichen amyloidosis were symptomatic.[12] Tay CH et al observed that 62.5% had itching whereas 37.0% were asymptomatic.[13] Kibbi AB et al found that 77% of macular amyloidosis and 73% of lichen amyloidosis had pruritis**.**[7] Al-Ratrout JT et al found that 71.43% had pruritis while 28.57% were asymptomatic.[10]

Al-Ratrout JT et al observed confluent macular pigmentation in 42.86%, rippled pattern of pigmentation in 23.81%, papules and hypopigmentation in 10% each.[6] Black MM et al observed that in 57.14%, the predominant lesion was macules.[10] In the present study pigmented macules with rippled pattern were seen in all (100%) cases of macular amyloidosis. In present study we observed pigmented hyperkeratotic papules in all (100%) cases of lichen amyloidosis and biphasic amyloidosis which is in concordance with study by Salim T et al and Ozkaya-Bayazit E et al who reported hyperpigmented hyperkeratotic papules and pigmentation in all cases of lichen amyloidosis.[9,12] Tay CH et al observed that 67.5% had papules, 22.5% had plaques 7.5% had macules and 2.5% had nodules. [13]

No association with any illness was found in patients with biphasic amyloidosis. Salim T et al studied the association of lichen amyloidosis with xerosis in 36.7%, diabetes mellitus in 16.7% of the patients. Looi LM in his study found systemic lupus erythematosus and scleroderma in 4.55% each.[8,12] Ortez-Romero E in his study found diabetes mellitus in 28.57%. Chronic active hepatitis was found in 14.29%.[14]

In our study all the 50 patient were recalled and were biopsied and histopathology was studied with reference to hyperkeratosis, hyper-granulosis, irregular acanthosis, basal cell liquefaction, melanin incontinence, and necrotic keratinocytes, irregular acanthosis Was seen in 17 patients, hyper-granulosis was seen in 12 patients, hyperkeratosis was seen in 12 patients, thining and elongation of reteridges was seen in 15 patients, papillomatosis was seen in 6 patients, inflammatory in-filterate was seen in 46 patients. Pigmentary incontinence was seen in 46 patients. Necrotic keratinocytes was seen in 39 patients. While basal cell liquefactive degeneration was seen in none of the patients. So the commonest finding seen were dermal changes i,e inflammatory infiltrate seen in macular amyloidosis followed by lichen and biphasic amyloidosis. Biphasic amyloidosis had both epidermal and dermal changes while lichen amyloidosis had mainly epidermal changes.

Salim T et al showed in their cases, epidermal changes of hyperkeratosis in 100% of their cases, acanthosis in 90% of the cases, papillomatosis in 33.3% of the cases, hypergranulosis in 16.7% of the cases and elongation of the rete ridges seen in 13.3% of the cases.[12] Amyloid deposits were detected in 28 out of 30 patients. Irregular acanthosis and increased granular layer was observed by Brownstein and Helwig et al in their study.[15] Amyloid deposition were however seen in the dermis as has been observed. The clue to final diagnosis and differentiation from other lesions rests in Apple green birefringence under polarised light on congo red staining.

CONCLUSION

Scrub, Hot water baths and other causative agents should be minimally used in patents with cutaneous amyloidosis for prolonged periods. Photo protection is must in them. Those with family history of cutaneous amyloidosis, adequate preventive measures should be adhered. Nodular cutaneous amyloidosis and sometimes lichen amyloidosis are associated with systemic amyloidosis. So such patents likely to develop systemic amyloidosis should be screen internally to rule out systemic amyloidosis.

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REFERENCES

1. Lachmann HJ, Hawkins DN. Amyloidosis and the skin. In: Woff K, Goldsmith LA, Katz SI, Gilchrist BA, Paller AS, Lefell DJ, eds. Fitzpatrick's Dermatology in General Medicine: 6th edn. Vol 2, Mc Graw Hill. 2008;1257-64.
2. Breathnach SM. Amyloid and Amyloidosis of skin. In: Burns T. Breathnach S, Cox N, Griffiths C, eds. Rook's Textbook of Dermatology: 7th edn. Vol 3, Oxford: Blackwell Science. 2004;57.36-57.51.
3. Bourke JF, Berth Jones J and Burns DA. Diffuse primary cutaneous amyloidosis. Br J Dermatol. 1992;127:641-4.
4. Wong CK. Cutaneous Amyloidosis. Int J Dermatol. 1987;26(5):273-7.
5. Wong CK. Lin CS. Friction Amyloidosis. Int J Dermatol. 1988;27(5):302-7.
6. Al-Ratrout JT, Satti MB. Primary localized cutaneous amyloidosis: A clinicopathologic study from Saudi Arabia. Int J Dermatol. 1997;36:428-34.

7. Kibbi AB, Rubeiz NG. Primary localized cutaneous amyloidosis. Int J Dermatol. 1989;31(2):95-6.
8. Looi LM. Primary localized cutaneous amyloidosis in Malaysians. Australias J Dermatol. 1991;32:39-44.
9. Ozkaya- Bayazit E, Kavak A, Gungor H, Ozarmagan G. Intermittent use of dimethylsuphoxide in macular and paular amyloidosis. Int J Dermatol. 1998;37:945-4.
10. Black MM. Primary localized amyloidosis of the skin: clinical variants, histochemistry and ultrastructure. In: Wegelius O, Pasternack A, eds. Amyloidosis. London Academic press. 1976;479-513.
11. Taheri R. Prevalence of macular amyloidosis in North Iran. 2007;52:192-3.
12. Salim T, Shenoi SD, Balachandran C, Lichen amyloidosis. A study of clinical, histopathological and immunofluorescence findings in 30 cases. Indian J Dermatol Venereol and Leprol. 2005;71:166-9.
13. Tay CH, Dacosta JL. Lichen amyloidosis: Clinical study of 40 cases. Br J Dermatol. 1970;82:129-36.
14. Ortiz-Romero PL. Clinicopathologic and Immunohistochemical studies of lichen amyloidosis and macular amyloidosis. Arch Dermatol. 1994;130:1559-60.
15. Brownstein MH, Helwig EB. The cutaneous amyloidosis: Localized forms. Arch Dermatol. 1970;102:8-19.

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