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CLINICOPATHOLOGICAL STUDY OF LICHEN AMYLOIDOSIS

Dermatology

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ABSTRACT

Background: Lichen amyloidosis is a type of primary localized cutaneous amyloidosis where there is deposition of amorphous amyloid substance in the dermis without the involvement of internal organs. It is not an uncommon disorder but there are only limited studies from south India.

Aim: To study the clinical features, demographic patterns and associations of lichen amyloidosis along with correlation of clinical and histopathological findings.

Methods: In this study, 30 patients with clinical diagnosis of lichen amyloidosis attending Dermatology clinic of a tertiary care hospital in South India were evaluated clinically and skin biopsy is taken for histopathological examination after an informed consent.

Results: A total of 30 patients were included in the study. Of the 30 cases, there were 19 males and 11 females. Majority of patients were in the age group of 31 – 50 years. Itching is the most common presenting complaint. Most of the patients (76.67%) had history of chronic friction and in few (10%) there was a positive family history. Pretibial region (96.67%) is the commonest site involved followed by forearm (26.63%) and arm (16.67%) in this study. Histopathologicaly hyperkeratosis and acanthosis were seen in all the cases, eosinophilic amyloid mass was seen in papillary dermis along with lymphohisticytic infiltrate in most of the cases.

Conclusion: Lichen amyloidosis is common in middle age with a slight male preponderance. Pretibial region is the commonest site of involvement and chronic friction has a major role in its development. Histopathology is helpful in confirming the diagnosis and usage of Congo red stain is more sensitive in detecting amyloid deposits.

KEYWORDS

lichen amyloidosis, papular amyloidosis, frictional amyloidosis

INTRODUCTION

Lichen amyloidosis is an extremely itchy skin condition characterized by development of multiple well defined papules which may show mild scaling and may form plaques by coalescing with nearby lesions. The lesions are usually hyper pigmented. It is the most common form of primary localized cutaneous amyloidosis which differs from systemic amyloidosis by the absence of deposition of amyloid in the internal organs.[1] The exact cause of lichen amyloidosis is not clearly known. Various etiological factors that have been proposed to be involved in the development of lichen amyloidosis include prolonged friction[2], genetic factors[3], chronic pruritus due to various causes[4] and viral infection.[5] It is usually seen over the extensor aspect of lower limbs but may also be seen over the extensor aspect of upper limbs, abdomen and dorsum of foot. Histologically there is deposition of amyloid protein in the papillary dermis along with epidermal changes. The response to various modalities of treatment is usually poor. The disease runs a chronic course which may last for many years.

Studies about lichen amyloidosis from South India are very limited. The present study is an attempt to highlight the clinical findings, demographic patterns and associations of lichen amyloidosis and to correlate the clinical features with histopathological findings.

MATERIALS AND METHODS

In this study, 30 patients with clinical diagnosis of lichen amyloidosis attending the Department of Dermatology were evaluated. The detailed history of each patient was noted with reference to age, sex, symptomatology, duration of skin manifestations, family history of similar lesions and usage of scrub. The duration of the cutaneous lesions, the size and its extent of involvement were noted.

All the patients were subjected to routine hematologic and standard biochemical investigations like complete haemogram, blood sugar, blood urea, serum creatinine, serum electrolytes, calcium and phosphate levels. Detailed urine examination was carried out in all of them. Skin biopsy was taken, specimens were stained with Haemotoxylin and Eosin (H&E) and special stain Congo red was used. Written informed consent was obtained from each patient. The study protocol was approved by the Institutional Ethical Committee.

OBSERVATIONS AND RESULTS

A total of 30 patients who were clinically diagnosed as lichen amyloidosis were recruited to the study of these 19 (63.33%) were male and 11 (36.67%) were female. Males outnumbered females. Male to female ratio was found to be 1.7:1. The age of these patients ranged from 26 - 77 years and most of the patients were in the age group of 31 – 50 years, with maximum number of patients in the 41 – 50 years (33.33%) followed by the 31 – 40 years (23.33%) age group. The duration of illness in this study ranged from 4 months to 11 years and majority of the patients had the lesions for more than 1 year duration.

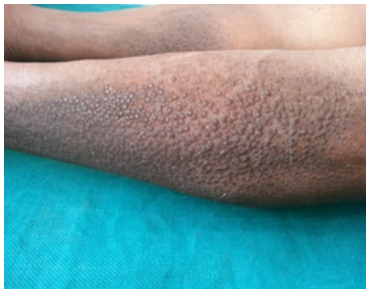

Figure 1: lichen amyloidosis involving shins

TABLE 1: BASELINE CHARACTERISTICS OF LICHEN AMYLOIDOSIS PATIENTS

Number of Patients	30
Mean Age (years)	48.13 (26-77)
Sex **Male**	63.33% (19)
Female	36.67% (11)
Duration of illness	Less than 6 months 13.33% (4)
	6 months – 1 year 20% (6)
	1 year – 2 year 26.67% (8)
	More than 2 years 40% (12)

Itching and raised skin lesions were the presenting symptom in majority (93.33%) of the patients but itching was absent in 2 patients (6.67%). Of the 30 patients with lichen amyloidosis most of the patients did not have a positive family history and only three (10%) patients gave history of similar lesions in other family members. In our study, 23 patients (76.67%) gave a history of using scrubs while taking bath and 7 patients (23.33%) denied history of any friction. Nylon scrub was used by maximum number of patients (60.86%). Coconut fiber was used by 4 (17.4%) patients and plastic brush by 5 (21.74%) patients.

In this study, all the patients had papules and hyperpigmentation. Confluent pigmentation was seen in 40% and reticulate pigmentation was seen in 60% of patients. Plaques were seen in addition to hyperkeratotic papules in 43.33% of patients. Nodules were seen in 3.33% of patients. In this study pretibial region is the commonest site (96.67%) affected by lichen amyloidosis. Involvement of forearm was seen in 26.63% and arms in 16.67% of patients. Involvement of back and thigh was seen in 10% of patients each. Other uncommon sites involved are chest & abdomen in 3.33% and gluteal region in 6.67%.

TABLE-2: DISTRIBUTION OF LESION

SITE	No. of patients	Percentage
Head and neck	0	0%
Chest and abdomen	1	3.33%
Back	3	10%
Gluteal region	2	6.67%
Arm	5	16.67%
Forearm	8	26.63%
Thigh	3	10%
Pretibial region	29	96.67%

In this study the most common systemic association seen with lichen amyloidosis was diabetes mellitus (16.67%) and hypertension (16.67%). Hypothyroidism and varicose veins were seen in 2 patients each. Follicular carcinoma thyroid was seen in one patient and one patient had bronchial asthma. In our study, 8 patients (26.67%) had xerosis. Chronic urticaria and eczema were seen in 2 patients (6.67%) each. PLE, vitiligo and acanthosis nigricans were seen in one patient each.

TABLE-3: ASSOCIATIONS OF LICHEN AMYLOIDOSIS

SYSTEMIC DISEASE	No. of patients	DERMATOLOGICAL DISEASE	NO. OF PATIENTS
Diabetes mellitus	5(16.67%)	**Xerosis**	8(26.67%)
Hypertension	5(16.67%)	**Chronic urticaria**	2(6.67%)
Varicose veins	2(6.67%)	**Eczema**	2(6.67%)
Hypothyroidism	2(6.67%)	**PLE**	1(3.33%)
Follicular carcinoma thyroid	1(3.33%)	**Vitiligo**	1(3.33%)
Bronchial asthma	1(3.33%)	**Acanthosis nigricans**	1(3.33%)

Histopathological examination revealed hyperkeratosis and acanthosis in all patients (100%). Papilomatosis was seen in 17 patients (56.67%), hypergranulosis in 14 patients (46.67%) and elongation of rete ridges in 9 (30%) patients. Basal cell degeneration was seen in 2 patients (6.67%). Amorphous, eosinophilic fissured mass of amyloid was seen in 26 patients (86.67%) in the papillary dermis. Other dermal changes seen were pigment incontinence in 23 patients (76.67%) and lymphohistiocytic infiltrate in 22 patients (73.33%).

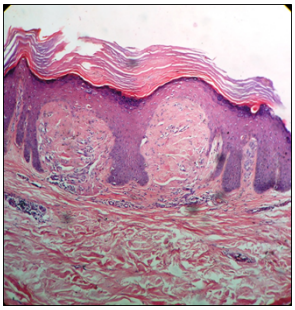

Figure 2: Histopathology of lichen amyloidosis

Special stain was done using Congo red for all the patients. Congo red revealed amyloid deposit in 93.33% of patients, while haematoxylin and eosin staining revealed amyloid deposits only in 86.67% of patients.

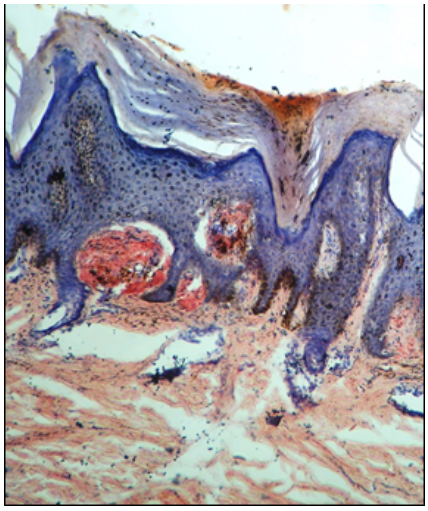

Figure 3: Congo red staining of lichen amyloidosis

DISCUSSION

Amyloidosis is the term used to describe a group of heterogeneous disorders characterized by the abnormal deposition of insoluble fibrillar protein material called amyloid in the extracellular spaces of various tissues and organs.6 The literal meaning of the word amyloid is 'starch-like' which has its origin from the Latin word amylum and the Greek word amylon.7 Gutman in 1928 was the first to describe the features of lichen amyloidosis. He described the case under the name “amyloidosis cutis nodularis et disseminata”. The name “Lichen amyloidosis” was given by Freudenthal in the year1930.8

Lichen amyloidosis is the most common subtype of primary cutaneous amyloidosis. Clinically patients will present with multiple hyperpigmented papules which are firm and discrete. Some of the papules may coalesce to form plaque. The lesions may show mild scaling. The lesions are usually persistent. Most common complaint of the patient is intense itching but few cases may occur without any itching9.

In this present study lichen amyloidosis was commonly found in the age group of 41 -50 years (33.33%) followed by 31 – 40 years (23.33%) age group. The mean age of the patients in this study was 48.13 years. Salim et al, in their study of lichen amyloidosis observed that the mean age of lichen amyloidosis patients was 43.13 years.10 Wong et al in their study observed that the most common age group affected with lichen amyloidosis was 40 – 60 years.11 In a study conducted by Ozkaya et al lichen amyloidosis was found to be common in the age group of 31 – 40 years and mean age of patients in their study was 43.5 years.12 Looi LM in his study of cutaneous amyloidosis observed that maximum number of patients with lichen amyloidosis was in the age group of 30 – 39 years with a mean age of 39.8 years.13

TABLE 4: MEAN AGE OF LICHEN AMYLOIDOSIS IN OTHER STUDIES

STUDY	MEAN AGE
Al-Ratrout JT and Satti MB14	43.7 years.
Salim et al10	43.13 years.
Looi LM13	39.8 years
Ozkaya et al12	43.5 years.
In this study	48.13 years

In the present study of 30 patients with lichen amyloidosis, the male to female ratio was 1.7:1, which is similar to studies by Salim et al (1.72:1) 10 and Ratrout JT et al (1.2:1) 14. Looi LM in his study observed a female preponderance (1:1.63).13 Tay et al15 and Ozkaya et al12 observed that incidence was almost equal in males and females. Most of the patients with lichen amyloidosis had their complaints for more than 1 year (66.67%), out of which 40% of patients had their complaints for more than 2 years. The duration of illness ranged from 4

months to 11 years which is similar to studies by Vijaya et al (2 months to 10 years) 16, Kibbi AG et al (few months to 16 years) 17 and Salim et al (6 months to 20 years).10

In this study of 30 patients with lichen amyloidosis, 28 patients (93.33%) patients had severe pruritus and 2 patients (6.67%) presented with skin lesions alone without any itching. Salim et al in their study of lichen amyloidosis observed that 10% of patients were asymptomatic without any itching.10 Al Ratrout JT and Satti MB reported that 18.18% of patients presented with skin lesions alone without any itching.14 Tay et al reported that pruritus was absent in a significant number of patients (37.5%). This study reported a higher number of patients with skin lesions but without any itching when compared with other studies.15 Our study is in accordance with the study conducted by Salim et al10 and Al Ratrout JT et al14 with pruritus as an important symptom seen in majority of the patients.

In this study 76.67% of patients gave a history of using scrubs while taking bath. Most of patients (14) used nylon sponge for scrubbing while others used plastic brush or coconut fiber.

Krishna et al in their study observed that history of chronic friction was present in 33.33% of patients with lichen amyloidosis.18 Salim et al in their study observed that 56.7% of patients with lichen amyloidosis reported the use of various scrubs. They also reported that nylon wire brush and coconut fiber were commonly used by south Indian people while taking bath.10 In contrast to other studies in this study we observed that history of chronic friction was seen in greater proportion of patients (76.67%) suggesting an important role in the etiology of lichen amyloidosis.

In this study 10% of patients had a positive family history of similar skin lesions which is quite similar to the other studies by Al Ratrout JT et al (11%)14, Krishna et al (11.11%)18 and Salim et al (20%)10 confirming that genetic factors may be involved in the development of lichen amyloidosis.

TABLE 5: FAMILIAL CASES IN VARIOUS STUDIES

STUDTY	PERCENTAGE
Salim et al10	20%
Al Ratrout JT et al14	11%
Krishna et al18	11.11%
PRESENT STUDY	10%

In this study pretibial region was the commonest site (96.67%) involved followed by forearm (26.63%) and arms (16.67%). Involvement of back and thighs were seen in 10% of patients each.

Vijaya et al in their study observed that pretibial area was the commonest site involved in lichen amyloidosis.[16] Al Ratrout JT and Satti MB in their study of cutaneous amyloidosis found that shins and forearm were the commonest site involved.[14]Ozkaya-Bayazit E.et al in their study observed that pretibial region was involved in all the patients (100%) of lichen amyloidsis.[12]Salim et al in their study found involvement of shin in 87.6% of cases, arms in 10% of cases and back in 3.3% of cases.[10]Tay CH and Dacosta JL in their study observed that 75% of patients had the involvement of shin, 15% had the involvement of thigh, 5% had involvement of forearm and 2.5% had involvement of back and arm.[15] In this study pretibial region was the commonest site involved which is in concurrence with most of the above studies. Forearm was the second most common site which is in concurrence with study conducted by Al Ratrout JT and Satti MB.[14] About 10% of patients had involvement of thigh which is similar to study by Tay CH and Dacosta JL.[15]

In this study one patient had lesions over chest, abdomen, back, upper and lower limbs sparing head, neck and intertriginous areas which is comparable to the generalized variant of lichen amyloidosis.[19]

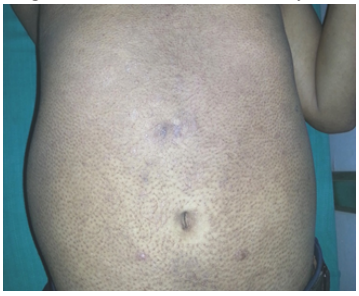

Figure 4: lichen amyloidosis lesions over chest and abdomen

Gluteal region is an uncommon site for lichen amyloidosis. In this study we observed gluteal region involvement in 2 patients. These patients had typical lesions of lichen amyloidosis in other sites also. Anosacral amyloidosis has been described as a separate variant in literature with the presence of lichenified plaques radiating from the anus to sacral area but our patients didn't have involvement of anosacral region.[20]

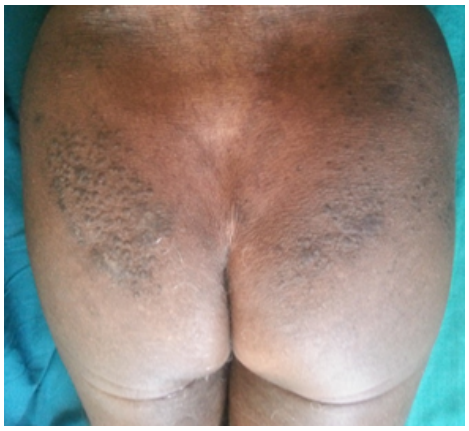

Figure 5: lichen amyloidosis involving gluteal region

In this study all the patients had hyperkeratotic papules and pigmentation. 40% of patients had confluent pigmentation and 60% had reticulate pigmentation. 43.33% of patients had hyperpigmented plaques along with papules. Nodules were seen in 3.33% of patients. Tay CH and Dacosta JL in their study of lichen amyloidosis reported that 67.5% had papules, 22.5% had plaques 7.5% had macules and 2.5% had nodules.[15] Ozkaya-Bayazit E et al in their study observed that all cases of lichen amyloidosis had papules and hyperpigmentation.[12] Salim et al in their study observed that 100% of patients had hyperpigmented papules while 60% of patients had plaques.[10] Al-Ratrout JT and Satti MB in their study found that among patients with lichen amyloidosis, 54.55% of patients had scaly pigmented papules while confluent pigmentation and reticulated pigmentation were seen in 27.27% each.[14] Morphology of the lesions in this study were comparable to the study conducted by Ozkaya-Bayazit E et al[12] and Salim et al[10] with all the patients having hyperpigmented papules and pigmentation.

In this study, lichen amyloidosis was associated with diabetes mellitus in 16.67% and hypertension in 16.67%. Hypothyroidism and varicose veins were seen in 6.67% of patients each. Follicular carcinoma thyroid was seen in one patient and one patient had bronchial asthma. Xerosis was seen in 26.67% of patients, chronic urticaria and eczema were seen in 6.67% of patients each. PLE, vitiligo and acanthosis nigricans were seen 3.33% patient each.

Salim et al in their study observed 16.7% of cases were associated with diabetes mellitus and 6.7% of patients had bronchial asthma. They reported malignancy in 6.7% of cases. They also observed that 36.7% of patients had xerosis.[10]

Lichen amyloidosis has been reported in association with medullary thyroid carcinoma in familial cases as a part of multiple endocrine neoplasia type 2.[21] In this study one case of lichen amyloidosis was found in association with follicular thyroid carcinoma. Lesions in this case appeared 3 months after the thyroid surgery and may be a casual occurrence. In this study 2 case of lichen amyloidosis were found in association with hypothyroidism. Gonul et al reported a case of generalized lichen amyloidosis in association with hyperthyroidism but cases have not been reported in association with hypothyroidism.[22] Wolf M had described one case of lichen amyloidosis associated with varicose veins. Lesions in that case were localized to the skin over varicose veins.[23] In this study 2 cases of lichen amyloidosis were seen in association with varicose veins but in these cases the lesions were not confined to the skin overlying the varicose veins. In this study one patient had depigmented macules and patches over dorsum of foot along with lesions of lichen amyloidosis over shins. This case is comparable to the case reported by Rajkumar et al, who observed a

case of cutaneous amyloidosis with hyperpigmented macules and papules over the pretibial region along with depigmented macules of vitiligo over abdomen and distal part of extremities.[24] Yalcin et al reported a case of generalized lichen amyloidosis associated with chronic urticaria.[25] In this study we observed two cases of lichen amyloidosis associated with chronic urticaria but these cases were not similar to the case reported by Yalcin et al. Association of diabetes mellitus and hypertension in this reflects the high prevalence of these conditions in India especially in South India and is comparable to the study conducted by Salim et al.[10] Other associations seen in this study might be of casual occurrence.

In this study the most frequent epidermal changes were hyperkeratosis and acanthosis which was seen in 100% of patients. Other epidermal changes seen were hypergranulosis (46.67%), papillomatosis (56.67%), elongation of rete ridges (30%) and basal cell degeneration (6.67%). Amyloid deposition in papillary dermis was seen in 86.67% of patients. Other dermal changes observed were pigmentary incontinence (76.67%) and lymphohistiocytic inflammatory infiltrate (73.33%). Congo red stain demonstrated amyloid deposits in 93.33% of patients.

Salim et al in their study observed that hyperkeratosis was seen in 100% of patients. Other epidermal changes were seen in various proportions which include acanthosis in 90%, papillomatosis in 33.3%, hypergranulosis in 16.7% and elongated rete ridges in 13.3%. Amyloid deposits were identified in 93.33% of patients, lymphocytic infiltrate was found in 70% of patients. Congo red stain revealed amyloid deposits in 100% of patients.[10] Al-Ratrout JT and Satti MB in their study found that all the cases of lichen amyloidosis revealed hyperkeratosis and hypergranulosis along with irregular acanthosis. Amyloid deposition in papillary dermis was also seen on all the cases. They have observed elongation of rete ridges and focal basal cell degeneration in few cases. They have reported a sensitivity of 90.90% with Congo red staining.[14] Epidermal changes seen in this study were comparable to the study conducted by Salim et al[10] and Al-Ratrout JT and Satti MB.[14] The dermal changes seen in this study were comparable to the study conducted by Salim et al. [10] The sensitivity of Congo red stain was similar to the study by Al-Ratrout JT and Satti MB. [14]

CONCLUSION

Lichen amyloidosis is an itchy skin condition common in fourth and fifth decade of life. It has a chronic course with chronic friction and genetic factors playing important role in its development. It commonly involves the pretibial region but occurs in other sites also. The association seen with follicular carcinoma thyroid and hypothyroidism needs further studies to substantiate the association. Histopathological examination is helpful in diagnosis and Congo red staining is more sensitive in detecting amyloid deposits.

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