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Original Research Article

A clinicopathological study of primary localised cutaneous amyloidosis

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ABSTRACT

Background: Amyloidosis is defined as extracellular deposits of heterogenic, misfolded proteins, amyloid fibrils, in various tissues. The term primary cutaneous amyloidosis (PLCA) usually includes macular amyloidosis (MA), lichen amyloidosis (LA) and nodular amyloidosis. Primary cutaneous amyloidosis is very common in Kerala probably due to socio-cultural practices. There has been no published data on PLCA from Kerala thus we undertook this study. The objectives of the study were to correlate clinical features of primary localized cutaneous amyloidosis with histopathologic findings; to evaluate the sensitivity of Congo red staining with polarized light in histopathologically proven primary localized cutaneous amyloidosis)
Methods: We undertook an observational analysis for a period of 2 years from May 2012 to April 2014 in the Department of Dermatology, Amrita Institute, Cochin. All cases clinically diagnosed as cutaneous amylodosis were included in the study. After informed consent, skin biopsy was taken. The histopathologic sections were stained with Congo red and seen under polarized microscopy for apple green birefrengance.
Results: A total of 70 patients were included in the study. Of the 70 cases, there were 20 males and 50 females. The most common clinical type was lichen amylodosis observed in 32 patients followed by macular amylodosis (28) and biphasic amyloidosis (10) cases. Histopathological compatibility was seen in 71% of MA and 89% cases of LA. Congored positivity was seen in 53.8%. Congored stain under immunofluorescence microscopy was done for 30 patients which gave a positivity of 85% which indicates that it is more sensitive that polarizing microscopy.
Conclusions: Our study showed that the most common type is lichen amylodosis. Histopathology and congo red staining with polarized light is a valuable aid in diagnosis. Congo red stain under immunofluorescence microscopy has greater sensitivity and improves the diagnostic yield.

Keywords: Amyloidosis, Congo red stain, Immunofluorescence

INTRODUCTION

Amyloidosis is defined as extracellular deposits of heterogenic, misfolded proteins called amyloid fibrils in various tissues. These deposits can be localized to a body site or can be systemic, involving several organs and tissues.[1] In primary localized cutaneous amyloidosis, deposition of amyloid occurs in previously normal skin with no evidence of deposits occurring in internal organs.[2] The term primary cutaneous amyloidosis (PLCA) usually includes macular amyloidosis (MA), lichen amyloidosis (LA) and nodular amyloidosis.

The exact etiology of PLCA is still unknown, familial predisposition and chronic friction is thought to have a role. The pathogenesis, also known as the "keratinocyte-

theory", is centred around inappropriate apoptosis of the keratinocytes with filamentous degeneration, which is later converted into amyloid material.[3]

Primary cutaneous amyloidosis, especially, LA and MA are very common in Kerala with steadily increasing incidence, probably owing to the socio-cultural practices. Since there has been no published data on PLCA from this part of the country, this study was undertaken being the foremost one.

METHODS

An observational analysis was conducted for a period of 2 years from May 2012 to April 2014 in the department of Dermatology, Amrita Institute of Medical Sciences, Cochin. All cases clinically diagnosed as cutaneous amyloidosis and willing for a skin biopsy were included in the study in which a detailed history was obtained from patients with stress on scrubbing, sunexposure, and atopic background. Exclusion criteria included those who were not willing for a skin biopsy. Skin biopsy was taken after obtaining informed consent. The histopathologic sections were stained with Congo red and visualised under polarized microscopy for apple green bi refrengence apart from the routine H&E stains. We also performed Congo red stain with immunofluorescence microscopy for some of the cases. The data was analysed using descriptive statistical tools including numerical frequencies and percentages.

RESULTS

A total of 70 patients who were clinically diagnosed as PLCA were recruited to the study. Of the 70 cases included, 20 were males and 50 females. The age ranged from 20 to 79 years with average of 49.5 years (Figure 1). The duration of the disease ranged from 6 months to 8 years. There was associated pruritis seen in 55 (78.5%) patients. The history of scrubbing was reported in 32(46%) patients. Lichen amyloidosis (LA) (Figure 2) was the most common clinical type observed in 32 patients (Table 1). It mainly involved the pretibial area (75%). The next frequently observed type was Macular amyloidosis (MA) (Figure 3) identified in 28 cases. The sites commonly involved were interscapular (18/28) followed by forearms (14/28). Biphasic amyloidosis was witnessed in 10 cases and it mainly involved the shin and forearm. Histo pathological examination (Figure 4) of haematoxylin and eosin stained sections of lichen amyloidosis showed hyperkeratosis, papillomatosis, mild acanthosis and elongated rete ridges. There was expansion of dermal papillae with globular deposits of eosinophilic, amorphous acellular material. Macular amyloidosis (Figure 5) showed amorphous deposits in the upper dermis without significant epidermal changes. Congo red stain (Figure 6) showed these deposits as reddish orange substance which when visualized under polarized light showed apple-green birefringence 3 cases of clinically suspected LA and 2 cases of MA demonstrated features of psoriasis. Histopathological compatibility was seen in 23 of 32 cases of LA and 25 out of 28 cases of MA (Table 2). Congo red positivity under polarized light was detected in 50% of LA and 52% of MA. Congored stain under immunofluorescence microscopy was done for 30 patients which gave a positivity of 85% which indiactes that it is more sensitive that polarizing microscopy (Table 3).

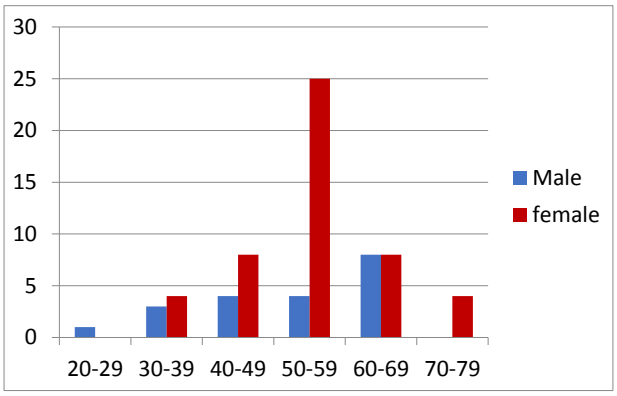

Figure 1: Age and sex distribution.

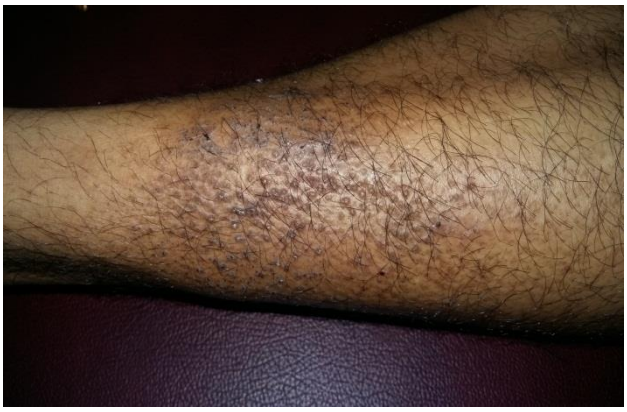

Figure 2: Lichen amyloidosis.

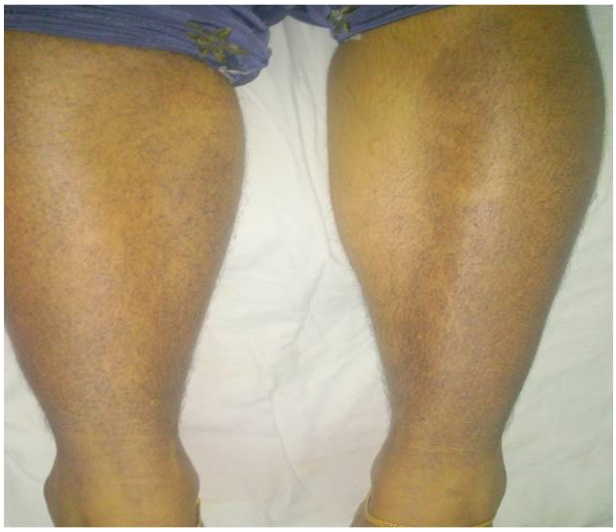

Figure 3: Macular amyloidosis.

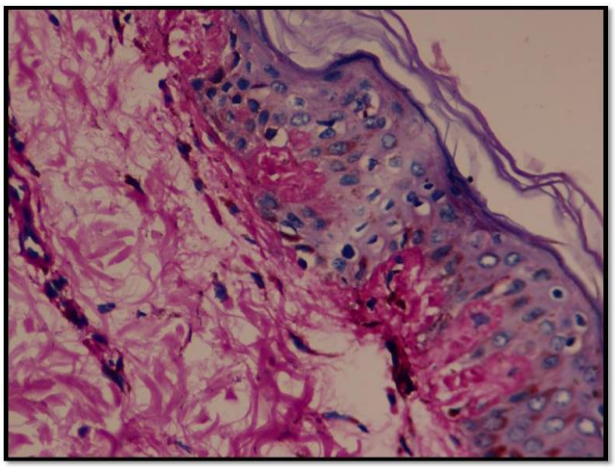

Figure 4: H & E section x 40 magnification showing hyperkeratosis, acanthosis and homogenous deposits in the upper dermis.

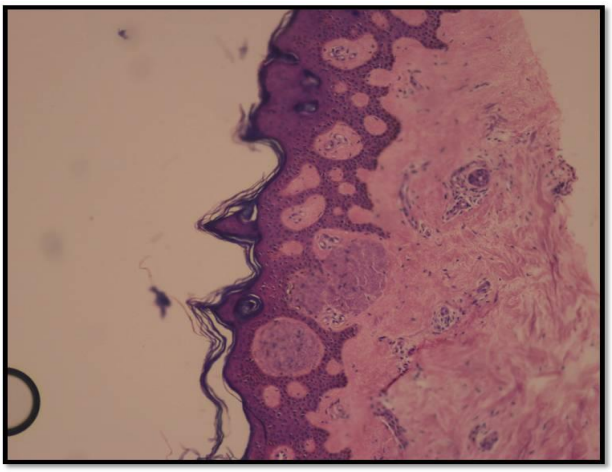

Figure 5: H & E section x40 magnification showing minimal epidermal changes and homogenous deposits in the upper dermis.

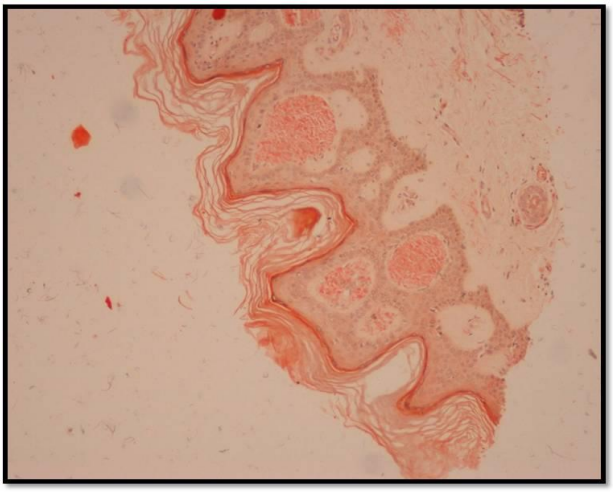

Figure 6: Congo red stain showing reddish orange deposits.

Table 1: Types of amyloidosis.

Type of amyloidosis	Frequency (%)
Lichen amylodosis	45.71
Macular amyloidosis	40
Biphasic amyloidosis	14.28

Table 2: Histopathological correlation.

Histopathological compatibility	Frequency (%)
Macular amyloidosis	71.87
Lichen amyloidosis	89.28
Biphasic amyloidosis	60-LA 40-LA+ MA

Table 3: Congored positivity.

Congored positvity	Frequency (%)
Macular	52
Lichen	58
Biphasic	50

DISCUSSION

Amyloid deposits are visualised as amorphous, eosinophilic, acellular material on routine hematoxylin and eosin staining. The congo-red stain gives an orange-red staining reaction to these deposits which show apple-green birefringence when examined under polarised light, this being the most important confirmatory test. This staining characteristic results from the cross-beta-pleated sheet conformation of the polypeptide backbones of the amyloid fibrils. These fibrils are ultra-structurally 8 to 12 nm in width and of indeterminate length.[1]

Amyloidosis can either be localised or systemic. The various forms of localised cutaneous amyloidosis are macular, lichen and nodular. Sometimes the features of LA and MA coincide and are known as biphasic amyloidosis.[4] Nodular amyloidosis is a rare condition. Secondary cutaneous amyloidosis is characterized by the presence of amyloid in the stroma of various cutaneous tumors such as basal cell carcinoma, squamous cell carcinoma, nevocellular nevi and a few adnexal tumours.[5] Secondary cutaneous amyloid deposits are also seen in seborrheic and actinic keratosis, Bowen's disease, porokeratosis, skin treated with UVA radiation after the ingestion of psoralens.[5]

Lichen amyloidosis was first described by Gutmann in 1928.[1] It is seen most frequently in South East Asia, China, and South America and is the commonest type of primary cutaneous amyloidosis. Albeit the etiology is unknown, chronic irritation to the skin has been proposed as an etiological factor.[5] Macular form of cutaneous amyloidosis was first described by Palitz and Peck in 1952.[6] MA has a characteristic female preponderance with the age of onset ranging between 21 and 50 years.[7]

Clinically, MA presents as poorly delineated hyperpigmented patches of grayish-brown macules with a rippled pattern, associated with deposition of amyloid material in the papillary dermis.

There is no convincing explanation for the origin of the amyloid protein in the skin. Still two theories namely, fibrillar body theory and secretory theory, have been proposed.[8] The fibrillar body theory states that damaged keratinocytes undergo filamentous degeneration by apoptosis and transformation by dermal fibroblasts and histiocytes that are converted into amyloid which deposits in the papillary dermis.[9] While secretion theory describes the deposition of amyloid from the degenerated basal keratinocytes at the dermoepidermal junction which eventually drops into the papillary dermis through the

damaged lamina densa of basal layer.[10] Chang et al suggested that keratinocyte destruction in cutaneous amyloidosis may occur as an initial result of apoptosis as apoptotic keratinocytes were seen in the spinous layer and the dermoepidermal junction just above the amyloid deposits.[11]

In our study the frequently encountered type was lichen amyloidosis which accounted for 46% of cases followed by macular amyloidosis which was detected in 40% cases and biphasic amyloidosis was seen in 14% cases. These findings were consistent with the findings of Vijaya et al where LA was the more common variant at 61.54%.[12]

Amyloid can be suspected on routine hematoxylin and eosin stain, and has to be confirmed by visualising congo-red stained slides under polarised light for apple-green birefringence. Eosinophilic deposits can also be due to hyalinised collagen. The histopathological compatibility was 92.3% in our study whereas other studies show 71%.[12] The sensitivity of congo-red staining in detection of amyloid was 53% in our study. However the study by Vijaya et al showed 100% sensitivity. In a study on macular amyloidosis by Bandlish et al the Congo red sensitivity was 26.6%.[13]

Though Congo red stain with apple-green birefringence under polarized light is the most popular method for detecting amyloid, it has limitations. Several studies have now found that examination of Congo red stain by fluorescent microscopy (FM) significantly enhances the diagnostic yield.[14] Fluorescent microscopy either is more sensitive in detection of the presence of a small amount of amyloid, which was otherwise missed by polarizing microscopy. In a study comparing the sensitivity of fluorescence microscopy with polarizing, microscopy in detection of amyloid in bone marrow biopsies they conclcuded that immunoflourescnt staing achieved 100% sensitivity, and congo red with polarising microscopy achieved 75% sensitivity.[15]

The present study has also shown higher sensitivity of immunoflourescent microscopy (85%) over polarizing microscopy (52%) in amyloid detection.

Mechanical trauma such as that induced by nylon fibers and bristles has been considered in the etiology of cutaneous amyloidosis and has been reported under various names, such as friction amyloidosis, towel melanosis and nylon clothes friction dermatitis 46% of our patients gave a history of using nylon scrubs or towels.[16]

The associations noted in our study were 27% and had concomitant polymorphous light eruption, 10% patients with LA had concomitant lichen simplex chronicus and 34.3% had diabetes mellitus. Lichen amyloidosis has been reported in connection with several skin disorders, including atopic dermatitis, lichen planus, and mycosis fungoides.[17-19]

The concomitance with polymorphous light eruption suggests that sunlight could be incriminated as a risk factor in the causation of PLCA in our patients. Eswara moorthy et al and Rasi et al, however, did not find any correlation between sun exposure and MA in their studies.[20,21] Epidemiologically, PLCA is prevalent in populations which generally have a high skin phototype (IV and V).[21] This might explain its rarity in western countries.

CONCLUSION

Our study showed that the most common type is macular amylodosis with interscapular region being the most important location. Histopathology and Congo red staining with polarized light is a valuable aid in diagnosis. However Congo red stain under immunofluorescence microscopy has greater sensitivity and improves the diagnostic yield.

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Ethical approval: The study was approved by the institutional ethics committee

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