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Panniculitis in Cutaneous Leishmaniasis: a Study in Sri Lanka

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ABSTRACT

Introduction: Panniculitis is the inflammation of subcutaneous Keywords: adipose tissue which is caused by many infectious and inflammatory conditions. It is high time to document panniculitis in the skin lesions with cutaneous leishmaniasis (CL) in Sri Lanka.

Objectives:This study was performed to assess demographic data and to describe panniculitis in patients with CL.

Methods: A descriptive cross-sectional study was done from 2013 to March 2018 at Teaching Hospital Kandy, Sri Lanka. The skin biopsies clinically suspected as CL evaluated histologically for diagnostic or indicative evidence of CL, and patients responded completely to the specific anti-leishmaniasis treatment were taken as the study population. Skin biopsies of 123 patients were assessed in view of dermal granulomata, Leishman-Donovan bodies and panniculitis.

Results: The majority of patients were in the age group of 36 to 50 years (N= 36:29.3%: mean=41.64 years: SD18.15 years) and there was a slight female predominance in the study (N=65:52.8%). A majority of skin biopsies revealed Granulomata (N=95: 77.2%). Leishmania Donovan bodies were identified among 43.1% of the lesions (N=53). Though there were 123 patients, only 66 (53.6%) skin biopsies were deeper enough to reveal subcutaneous tissue. A significant amount of skin lesions showed subcutaneous tissue inflammation (N=59:89.39%), predominantly non-granulomatous in morphology (N=44:74.6%).

Conclusion: Subcutaneous tissue inflammatory infiltrate in the non-granulomatous morphology is an important feature of the skin biopsies of CL especially in the granulomatous variant of the CL, which can be achieved by a deeper elliptical biopsy.

Cutaneous leishmaniasis, Panniculitis, Subcutaneous tissue, Granulomata, Leishman-Donovan bodies.

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Introduction:

In the nineteenth century, a new parasite identified which causes leishmaniasis by several scientists individually, who are Cunningham, Borovsky, Leishman, Donovan, Lindenberg and Vianna [1]. In 1903, the specific term "Leishmania" was coined by Ronald Ross Thereafter the clinical. geographical, sociodemographic and histopathological features of the disease human were supplemented by various studies.

Cutaneous leishmaniasis (CL) is an important public health problem in several parts of the world including Sri Lanka [3]. It is a zoonotic disease that transmitted through an infected female sand fly [4]. Though the clinical diagnosis can be done by an experienced practitioner in an

endemic region, it could mimic some other conditions [5]. There are various laboratory techniques to diagnose CL. Punch skin biopsy is widely used and a popular diagnostic procedure [6].

Panniculitis is the inflammation of subcutaneous adipose tissue which causes by many infectious pathogens such as bacteria, fungi and parasites, and some inflammatory conditions. However, only a few articles emphasize the presence of panniculitis in CL [7, 8]. The aim of this study was to assess panniculitis and its morphology in the skin biopsies of patients with CL and to correlate it with dermal granulomata and discernible Leishman-Donovan bodies, in Sri Lanka.

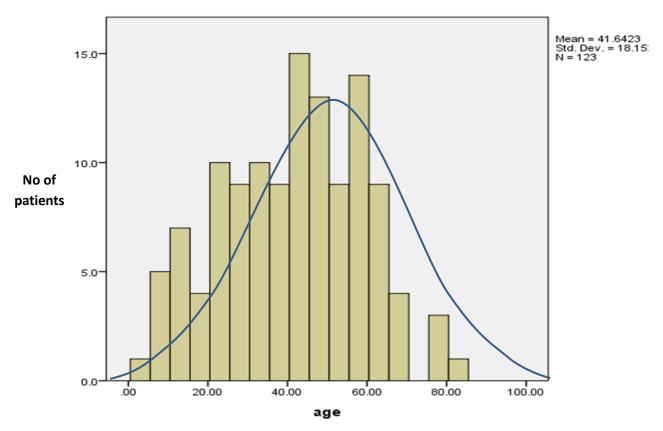


Figure 1: Histogram showing the distribution of age of the patients with cutaneous leishmaniasis.

Methods:

A descriptive cross-sectional study of 123 cases from 2013 to March 2018 at Teaching Hospital Kandy, Sri Lanka. The skin biopsies clinically

suspected as CL were assessed for histological evidence of CL and the biopsies with LD bodies were taken as diagnostic cases and biopsies with well or ill-formed granulomata with plasma cells were assessed for complete response to specific anti-leishmaniasis treatment and were considered as the study population. Demographic data were obtained from the pathology request forms and clinic record. Formalin-fixed, routinely processed, paraffin embedded, 4-5-micrometer thick histology sections, stained with haematoxylin & eosin (H &E) and special stain Giemsa were examined to re-assess histomorphological features and to highlight the LD bodies.

The skin biopsies with subcutaneous tissue were assessed for the presence of inflammation and when it present whether granulomatous or non-granulomatous in morphology. Further, the presence of Leishmania-Donovan (LD) bodies and dermal granulomata were evaluated to correlate with the panniculitis.

Results:

One hundred twenty-three (123) units were studied. Mean and SD values were used to describe the continuous variables and percentages and chi-square test for categorical variables. Risk association was described by using the Odds Ratio. 95% confidence interval and probability level less than 0.05 were used for statistical significance.

Age of the patients with CL is demonstrated in figure 1. It ranged from 3 years to 83 years (Mean=41.64 years: SD=18.15 years). Distribution of age showed the typical Gaussian distribution of biological parameters. The majority of the participants were in the age group between 36 years to 50 years (N= 36:29.3%).

Table 1: Distribution of age and sex of the patients with CL

Age category	Number (N)	Percentage (%)
<20	17	13.8
21-35	30	24.4
36-50 51-65	36	29.3
>66	32	26.0
	08	06.5
Sex category		
Male	58	47.2
Female	65	52.8
Total	123	100

There was a slight female predominance in the studied patients (N=65:52.8%) and the majority

belonged to the age group 36 years to 50 years which were not statistically significant (P>0.05).

Table 2: Distribution of dermal granulomata and visible parasites in the skin biopsies of patients with CL.

Granulomata	Number (N)	Percentage (%)	
Present	95	77.2	$X^2 = 29.77$
Absent	28	22.8	P<0.001
Parasites			
Present	53	43.1	
Absent	70	56.9	
Total	123	100.0	

Table 2 describes the distribution of dermal granulomata and discernible parasites in the skin lesions among patients with CL. Majority displayed granulomata (ill or well-formed) in the dermis (N=95:77.2%) which was statistically significant (p<0.05). The parasites of CL were clearly identified among 43.1% of the lesions (N=53) either with basic H & E slides or Giemsa

special stain. LD bodies were typically identified within the dermal histiocytic infiltrate (Figure 2). Parasites within the keratinocytes of the epidermis were also identified in a few cases (Figure 3). Even though the LD bodies are usually seen in non-granulomatous inflammation, some granulomatous lesions also showed organisms (N=39:41%).

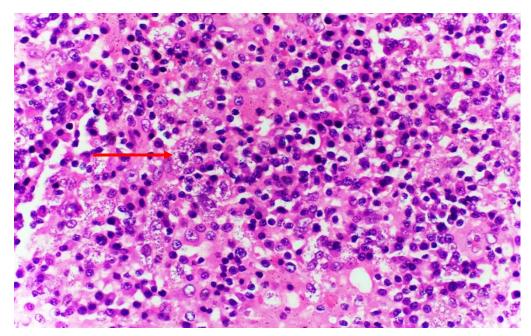


Figure 2: Photomicrograph showing Leishmania-Donovan bodies in the dermain macrophages, haematoxylin & eosin x400.

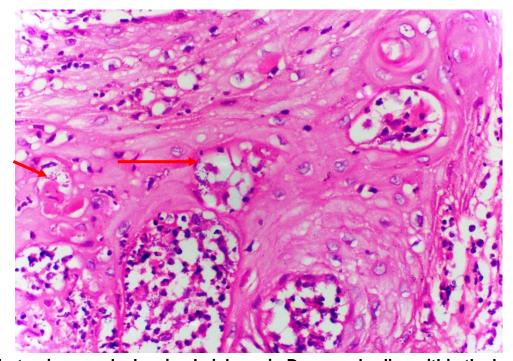


Figure 3: Photomicrograph showing Leishmania-Donovan bodies within the keratinocytes of the epidermis, haematoxylin & eosin x400.

Table 3: Distribution of panniculitis in the skin biopsies of CL

Panniculitis	Number (N)	Percentage (%)	X ²	P value
Present	59	89.4	40.97	P<0.001
Absent	07	10.6		
Total	66	100		

Though there were 123 skin biopsies of CL only 66 biopsies reach the subcutaneous tissue to assess inflammation. Table 3 describes the inflammation of the subcutaneous tissue in CL. Subcutaneous tissue inflammation was detected

in 89.4% (N=59) of cases and absent in 10.6% (N=07). The presence of subcutaneous tissue inflammation was statistically significant (X^2 40.97: p<0. 001).

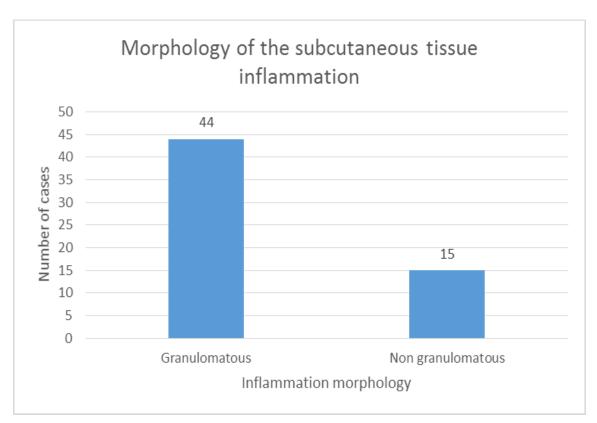


Figure 4: Bar chart showing the distribution of the morphology of panniculitis in patients with CL

A significant amount of the skin lesions (X^2 14.254: p<0.05) with subcutaneous inflammation showed non-granulomatous inflammation (N=44:74.6%) (Figure 5).

Granulomatous panniculitis was present in 28% of the skin lesions (N=15:25.4%) (Figure 6). Categorization of panniculitis as septal, lobular and mixed was not done.

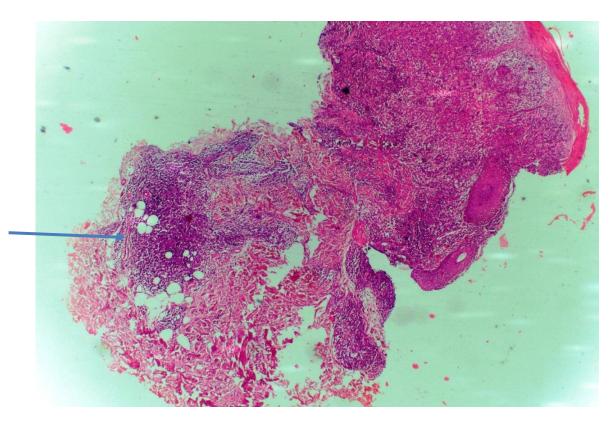


Figure 5-A: Photomicrograph showing non-granulomatous inflammation in the subcutaneous tissue, haematoxylin and eosin x40.

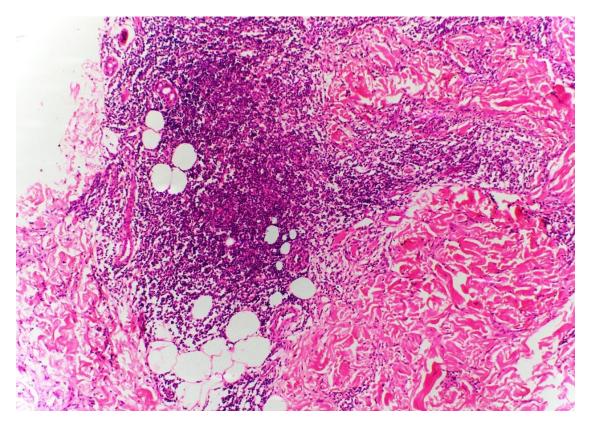


Figure 5-B: Photomicrograph showing non-granulomatous inflammation in the subcutaneous tissue, haematoxylin and eosin x100.

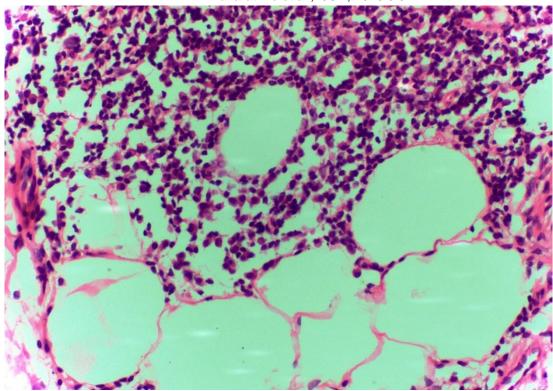


Figure 5-C: Photomicrograph showing non-granulomatous inflammation with plasma cells in the subcutaneous tissue, haematoxylin and eosin x400.

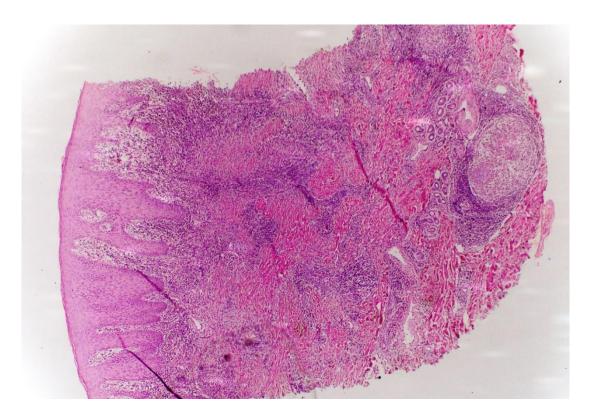


Figure 6-A: Photomicrograph showing granulomatous inflammation in the subcutaneous tissue, haematoxylin and eosin x40.

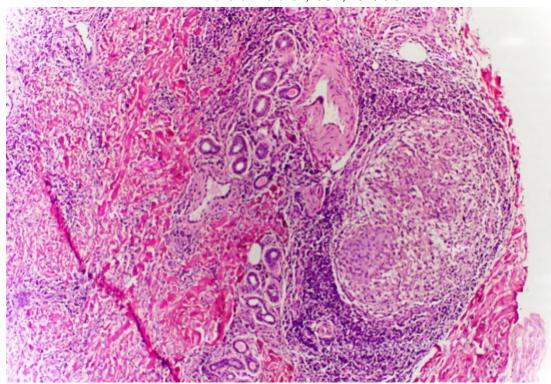


Figure 6-B: Photomicrograph showing granulomatous inflammation in the subcutaneous tissue, haematoxylin and eosin x100.

Table 4: Correlation of the dermal granulomata and panniculitis in the skin lesions of CL

	Granulomata	Present	Absent	Total
Panniculitis				
Present		55	05	60
Absent		04	02	06
Total		59	07	66

OR =5.500 (95% CI = 0.799 - 37.837)

The relationship between dermal granulomata and panniculitis is described by this table. Panniculitis was evident as a characteristic feature in the granulomatous variant of CL and it is statistically significant (OR=5.500).

Table 5: Correlation of the discernible LD bodies and panniculitis in the skin lesions of CL

LD bodies	Present	Absent	Total
Panniculitis			
Present	30	29	59
Absent	02	05	07
Total	32	34	66

Table 5 demonstrates the association between panniculitis and discernible LD bodies in the skin lesions of CL. There is no significant association panniculitis and discernible LD bodies and almost equal numbers of patients either absence or presence of discernible organisms show panniculitis.

Discussion:

Cutaneous leishmaniasis (CL) is an important public health problem which displays a wide range of clinical and histological findings [9]. Histological assessment of the skin lesions plays a principal role in the diagnosis. This study was to assess demographic data and to evaluate panniculitis in CL.

Age distribution of the patients of CL ranged from 3 years to 83 years and that represents the normal distribution. The majority of patients were in age group from 36 to 50 years with a mean of 41.64 years which include working age population. Many studies showed a male preponderance, but the present study demonstrated a slight female predominance.

In histological perspective, the characteristic feature of the skin biopsies of CL includes a dense chronic inflammatory infiltrate with or without amastigotes to a variable degree of granulomatous inflammation throughout the dermis [5, 9]. The inflammatory infiltrate might extend into the deeper subcutaneous tissue, which regards as panniculitis. Panniculitis is an important histological finding because it could simulate other skin diseases such as chronic skin infections, discoid lupus erythematosus, and cutaneous lymphoma [7, 8]. In the present study, it was identified in a significant amount of skin biopsies with CL, mostly granulomatous in nature. Sharquie et al from Iraq also highlight the presence of panniculitis in the lesions with CL, however, the morphology of the inflammation was not appraised [7]. Further significantly panniculitis is evident granulomatous dermatitis of CL. granulomata could identify in a variety of skin conditions and panniculitis is a good feature to support the diagnosis of CL.

Phenotypically, the presence of Leishmania-Donovan (LD) bodies in the skin biopsies is a confirmatory finding, though it might not be a constant finding [5]. The present study, only 43.1% of the study units contained parasites even with special stains. However, cases without discernible parasites responded to the treatment well. The LD bodies were mostly noted dermis within macrophages extracellularly. In a few cases, the organisms were noted in the keratinocytes of the epidermis. which indicate trans-epidermal elimination of the organisms (15). Accordingly, even superficial biopsies could evaluate for the diagnosis of CL. None of the skin biopsies demonstrates organisms in the subcutaneous tissue. Hence panniculitis could consider as a part of the inflammatory reaction of CL. In the present study, the association between discernible parasites and panniculitis was assessed and reveals no relationship.

Conclusions

Subcutaneous tissue inflammatory infiltrates in non-granulomatous morphology is an important feature of the skin biopsies of CL in Sri Lanka which suggest a deep elliptical biopsy in the future. Further panniculitis is strongly associated with dermal granulomata but not with LD bodies in CL.

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.Conflict of Interests:

There are no conflicts of interest.

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