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Original Research Article

A Study of Clinico-Histological Correlation in TT, BT, BB, BL and LL Leprosy Patients in a Tertiary Care Centre

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Abstract

Introduction: Leprosy is an infection caused by *Mycobacterium leprae* that affects the skin and nerves. The presenting features of leprosy include macules and papules, anesthesia or paresthesia over lesions, neuritis and reactions that vary in each leprosy patient. Histological features of skin biopsy are an important tool in diagnosing leprosy and determining the type of leprosy. Clinical and histopathological findings in leprosy vary according to the immunological status of each patient.

Aim: To study clinical and histopathological correlation among the newly diagnosed leprosy cases.

Materials and Methods: Twenty-one untreated clinically diagnosed cases of leprosy between December 2022 to November 2023, classified according to RIDLEY AND JOPLING`S (1966) classification system were included in the study. Hematoxylin & Eosin (H & E) and Fite-Faraco staining techniques were used. Upon confirmation, the diagnoses were correlated, concordance and discordance were noted and analyzed.

Results: In this study, the male to female ratio was 1.3:1. The most commonly affected age group was 31-40 years and maximum clinic-histopathological correlation was seen in lepromatous leprosy (75%) followed by tuberculoid leprosy (66.66%). Fite-Faraco stain was positive only in 6 cases (28.57%).

Conclusion: Clinico-pathological correlation is maximum in polar groups as they are stable. However, maximum disparity is seen in borderline cases as they have histopathological changes that vary based on different sites as well as different lesions in the same patient.

Keywords: *Mycobacterium leprae*, Leprosy, A Ridley-Jopling Classification.

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Introduction

Leprosy is an infectious disease caused by *Mycobacterium leprae* or Mycobacterium lepromatosis.[1] Nasal Mucosa is considered the major entry point for lepra bacilli.[2] It primarily affects the peripheral nervous system, skin and damage to vital organs such as eyes, larynx, testes, and bones may occur.[1,2]

Schwann cells of peripheral nerves are the first resting place for lepra bacilli. *M. leprae* have a predilection for cooler areas of the body.[3]

The diagnosis and classification of leprosy have traditionally been based on the clinical examination, with additional information from slit skin smears and histopathological examination.[4,5] Leprosy has a wide spectrum of clinical presentation and poses a diagnostic challenge, especially in the early stages. The study of histo-pathological changes in leprosy has contributed a great deal to the understanding of the disease.[6,7]

Based on Ridley and Jopling`s (R&J) Classification, each patient with leprosy can be further classified into various sub-types like TT(Tuberculoid), BT(Borderline tuberculoid), BB(Mid borderline), BL(Borderline lepromatous), LL(Lepromatous) by observing clinical findings, histological features and bacteriological index(BI) of the patient.[7]

Due to variable clinical and histopathological findings, often disparities while correlating the two have been observed. Clinico-pathological correlation has provided insights into varied manifestations and complications of the disease.

Aim and Objectives: To study the clinical and histopathological correlation among the leprosy cases.

Materials and Methods

This is a descriptive cross-sectional study conducted in the Department of Dermatology, Venereology and Leprosy at Dr. M. K. Shah Medical College, Ahmedabad for a period of 1 year from December 2022 to November 2023. After taking written informed consent, 21 untreated patients from all age groups where leprosy was suspected based on the skin lesion morphology and nerve involvement were included.

Relapse cases, lepra reaction cases, cases of pure neuritic leprosy and patients who did not consent for skin punch biopsy were excluded. A detailed history with cutaneous examination in reference to leprosy was done in all cases. The number, morphology and distribution of skin lesions and other features like leonine facies, and ear lobe infiltrations were observed. The peripheral nerves were palpated for any thickening, nodulation, tenderness, or abscess formation. Sensory and motor examination was performed. Slit skin smears from lesional sites, one from each eyebrow and earlobe were taken and the bacteriological and morphological indices were recorded.

Compiling the clinical and bacteriological findings, the clinical spectrum of each case was identified. For the classification of spectral groups Ridley and Jopling's classification was adopted. After prior consent from patients, skin biopsies were performed using a 4mm disposable biopsy punch from a representative skin lesion prior to commencement of treatment and sent for histopathological examination. Skin biopsy specimens fixed in 10% formalin were processed and multiple sections were taken. The Hematoxylin-Eosin and Fite-Faraco staining for lepra bacilli were done for each biopsy section. A histopathological spectral typing was done based on epidermal and dermal changes, type of granuloma, characteristics of infiltrate and findings obtained from Fite-Faraco staining. In this study, the leprosy cases were grouped as per Ridley and Jopling's (1966) classification into tuberculoid leprosy, Borderline tuberculoid leprosy, Mid Borderline leprosy, Borderline lepromatous leprosy and Lepromatous leprosy. Descriptive statistics were produced for demographic, clinical and laboratory characteristics for 21 patients enrolled in the study. All other cases as well as those who did not give written informed consent were excluded from the study. The extent of correlation between the clinical and histopathological spectrum was assessed. Quantitative and qualitative variables were analyzed and summarized as counts and percentages.

Results

The study included patients from 11 years to 63 years of age. A maximum of 52.38% (n=11) of patients belonged to the age group of 31-40 years. There were 57.14% (n=12) males and 42.85%(n=12) females and the male to female ratio was 1.3:1. After clinical examination of all 21 clinically diagnosed leprosy cases, 38.09%(n=8) were of lepromatous type, 23.80%(n=5) were observed to be borderline lepromatous, 4.28%(n=3) were of the mid-borderline and tuberculoid type each and 9.52%(n=2) were of borderline tuberculoid type.[Fig.1] 57.14%(n=12) of patients showed positive findings in slit skin smear. On histopathological examination, epidermal atrophy was the most common finding which was present in 85.71% (n=18) of patients Grenz zone was found in 52.38% (n=11) of patients, peri-appendageal inflammatory infiltrates were observed in 42.85% (n=9) of patients, foamy macrophages were seen in 19.04% (n=4) of patients and Fite-Faraco staining showed scattered rods and clumps in 28.57%(n=6) of patients. Histopathological examination showed changes suggestive of lepromatous leprosy in 38.09%(n=8), Borderline lepromatous leprosy in 23.80% (n=5), Mid borderline in 4.76%(n=1), borderline tuberculoid leprosy in14.28%(n=3) and Tuberculoid leprosy in 19.04% (n=4) of the patients.

Table 1: Clinical and histopathological correlation.

Clinical Diagnosis	Total	Histopathological diagnosis					Positive Correlation (%)
		TT	BT	BB	BL	LL	
TT	3	2	0	0	0	1	66.66%
BT	2	1	1	0	0	0	50%
BB	3	1	1	1	0	0	33.33%
BL	5	0	1	0	3	1	60%
LL	8	0	0	0	2	6	75%

Among the eight clinically diagnosed cases of Lepromatous Leprosy (LL), histopathological spectral correlation was seen in six cases (75%). In the remaining two patients (25%), histopathological findings correlated with the borderline lepromatous type (Table-1). Clinico-histopathological correlation was seen in three out of five patients of borderline lepromatous leprosy (60%) and one out of three patients of mid-borderline leprosy (33.33%). 50% patients of borderline tuberculoid and 66.66% of tuberculoid showed a positive correlation in the correlation study. LL cases showed maximum concordance and BB cases showed maximum discordance in our study.

Discussion

Leprosy shows a wide variety of clinical and histopathological features. The clinicopathologic correlation studies have provided further insights into the disease, its varied clinical and histopathological manifestations and its complications.

In our study, leprosy was slightly more common in males, with a male-to-female ratio of 1.3:1, which is similar to the study done by Tiwari et al. Illiteracy, lack of awareness and knowledge, various social factors along with strong cultural practices contribute to the under-reporting of leprosy cases among females.[8] A maximum number of cases were seen within the age group of 31- 40 years with the youngest patient being 11 years of age and the oldest patient being 63 years of age. These findings were analogous to a study done by Chanda et al which showed a lower incidence of leprosy among children.[9] The increased number of cases in older age groups and decreased cases in children indicate a decreasing incidence of leprosy in the population.

In our study, LL cases showed a maximum clinico-pathological correlation (75%) which was followed by TT leprosy (66.66%). Cases of BB leprosy showed minimum correlation (33.33%). On the contrary, 80% of LL cases and 50% of BB cases showed a positive correlation in the study done by Sankar et al and Moorty et al.[10,11] More discordance was seen in the Mid borderline suggesting that the BB subtype of leprosy is a more unstable type than the LL and TT subtypes.

We observed that 28.57% had positive findings on Fite-Faraco stain which is less compared to the study done by Tiwari et al and Chanda et al, where they found positive results in 55% and 38% respectively.[8,9]

The overall positive correlation in our study was 61.90% similar to the study done by Moorthy et al, Mitra et al and Bhatia et al.[11,12,13] In the study done by Sehgal et al, only 33% positive correlation was seen. Results obtained from various clinico-histopathological correlation studies done previously are shown in Table-2.

Table 2: Clinico-pathological correlation reported in various studies.

Similar studies done in the past	Overall correlation between clinical features and Histopathology (%)
Tiwari et al[8]	54%
Chanda et al[9]	48.10%
Mitra et al[12]	57.16%
Sehgal et al[14]	33%
Bhatia et al[13]	69%
Moorthy et al[11]	62.63%
Our study*	61.90%

[*Only TT, BT, BB, BL, LL included in our study]

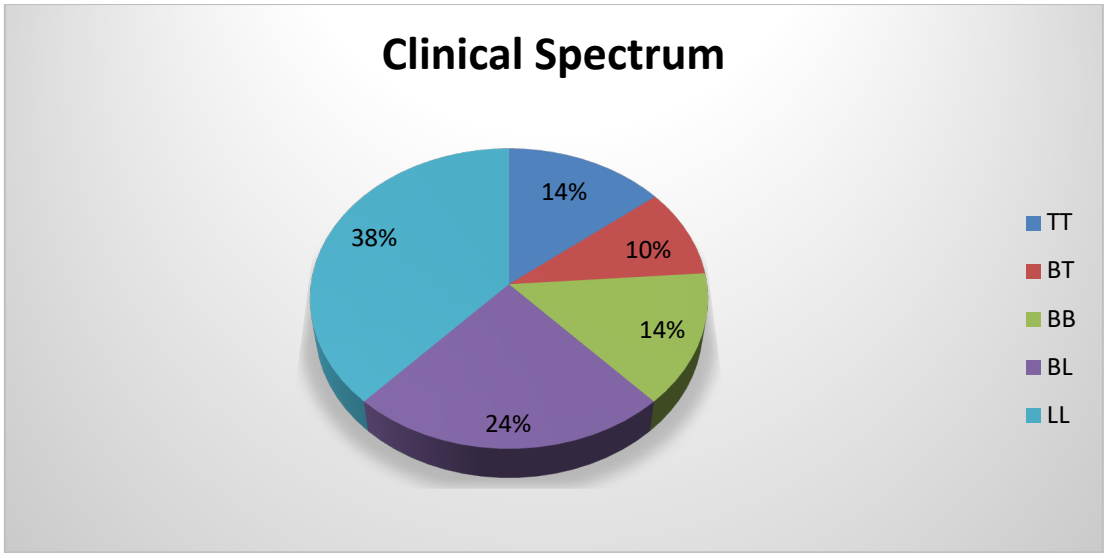

Figure 1: Clinical spectrum.

Figure 2: (a) Single, well defined, erythematous to violaceous, infiltrated plaque (2.5X3.5 cm) over left malar area of face, with thickened right Greater auricular nerve and bilateral ulnar nerves having rope-like consistency and absent tenderness. (B)Specimen stained with H&E, 40x magnification showing and peri-appendageal dermal inflammatory infiltrates and nodular accumulation of foamy macrophages in upper dermis . Here the clinical findings were suggestive of TT leprosy but the HPE findings corroborated with LL type.

The variation in different studies may be due to inter-observer variation, both clinically and histopathologically.

A disease like leprosy needs an appropriate classification system and the most widely accepted classification system by researchers is that given by Ridley and Jopling which primarily takes into consideration the immune status of the individual along with clinical, histopathological and bacteriological findings. Despite having such an accurate classification system, leprosy cases have shown additional variations while correlating the clinical and histopathological features as the clinical classification gives recognition only to the gross appearances of the lesions, while histopathological classification varies according to the immune response of the tissue which is more precise and well defined.

This can be justified by one of the cases that we encountered during this study whereby a 36-year-old male presented with a Single, well defined, erythematous to violaceous, infiltrated plaque (2.5X3.5 cm2) smooth and shiny surface along with overlying loss of sensation over left malar area of face. [Fig.2(A)] Absence of bacilli on SSS and lesion morphology pointed towards TT leprosy. However, HPE showed thin and atrophied epidermis with flattening of rete ridges, a clear sub-epidermal Grenz zone, peri-appendageal granuloma with foamy macrophages and peri-appendageal

infiltrate of lymphocytes in upper dermis which were suggestive of LL.[Fig.2(B)]

Furthermore, analyzing serial biopsies from either the same lesion or paired lesions is fundamental for better clinico-histopathological correlation. The high proportion of multibacillary (MB) leprosy cases in our study aligns with global trends and previous research findings of Tiwari et al; 2011.[8]

MB leprosy, with its higher bacterial load, poses a greater risk of transmission and is more likely to cause severe complications and deformities if not promptly managed. Despite advances in elimination efforts, the continued prevalence of undetected MB cases, often due to atypical presentations, highlights the need to improve active case detection and early diagnosis.

Histopathological correlation studies are crucial as additional findings that are reported from these studies remain essential for refining classification systems so that simplified and advanced approaches for disease identification can be devised and eventually diagnostic accuracy can be enhanced. This can lead to improved and streamlined detection of cases that could otherwise be missed or misdiagnosed. Thus, overall prognosis can be improved.

Conclusion

There is a wide variation in the clinical as well as the histopathological patterns of leprosy and there often occurs disparity and deviation while correlating the clinical and histopathological features. Clinico-histopathological studies are essential as they provide a better understanding of the disease as well as help us to understand the immunological status and infectivity of each patient.

Ethical Approval: Approved

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