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Original Article

Evaluation of Leprosy Cases in Correlation of Histopathology and Demonstration of Lepra Bacilli: A Prospective Study

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Abstract

Introduction: The main feature of the vast majority of leprosy biopsy specimens is a granulomatous infiltrate that has different features according to the form of leprosy, the time and site of the biopsy, the presence of a leprosy reaction, and therapy.

Aim: This study aims to analyze the clinicohistopathological correlation in different types of leprosy.

Materials and Methods: Skin biopsies were taken from clinically suspected patients. The tissue section was stained routinely by hematoxylin and eosin. A special stain like modified Fite-Faraco (FF) was done to demonstrate lepra bacilli. Histopathological findings were graded into tuberculoid, borderline tuberculoid, midborderline, borderline lepromatous (BL), and lepromatous (LL), according to Ridley and Jopling scale. The clinicohistopathological correlation was done.

Results: In 162 cases, 154 cases were confirmed as leprosy in histopathology. LL leprosy was more common 26.6% followed by BL leprosy 25.3%. In histopathologically confirmed leprosy cases, 103 cases (67.6%) were positive in FF stain.

Conclusion: Some degree of overlap between different types of leprosy, both clinically and histopathologically, correlation of clinical and histopathological features along with bacteriological index appears to be more useful for accurate typing of leprosy than considering any one of the single parameters alone.

Key words: Fite-Faraco stain, Histopathology, Leprosy

INTRODUCTION

Leprosy is caused by *Mycobacterium leprae*. Most people infected with this organism are thought not to develop clinical disease, although there are no tools to diagnose subclinical infection. *M. leprae* is slow growing and the incubation period of leprosy is long at 2–12 years. The mode of transmission is still not conclusively proven, although person-to-person spread through nasal droplets is believed to be the main route.[1]

The prevalence has fallen substantially in the past 50 years,[2] but transmission continues and leprosy remains a public health problem.[3] Various hindrances remain to reduce this prevalence further. The mode of transmission of leprosy is not well understood, although it is probably person to person through nasal droplets.[1] How many infected people develop clinical disease and whether reactivation of the past infections is important are unknown.

The World Health Assembly passed a resolution in 1991 to "eliminate leprosy as a public health problem" by 2000; it defined elimination as reducing prevalence to less than one case per 10,000 population.[4]

The genome sequence of *M. leprae* has been available since 2001. Work on strain typing of *M. leprae* has used either single-nucleotide polymorphisms or short or variable number tandem repeat genotyping. Early work with single-nucleotide polymorphisms revealed four subtypes of *M. leprae* and postulated a route of spread around the world.[5]

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Infection with *M. leprae* leads to chronic granulomatous inflammation in the skin and peripheral nerves. The type of leprosy that patients develop is determined by their cell-mediated immune response to infection. Types may be categorized according to the Ridley-Jopling classification,[6] which is based on skin lesion type and bacterial load. Patients with the tuberculoid (TT) disease have a good cell-mediated immune response and few lesions with no detectable mycobacteria. Patients with little or no resistance toward *M. leprae* develop lepromatous (LL) leprosy have multiple lesions with the high bacillary load. Between these two classifications are the borderline leprosy types, in which patients have some cell-mediated immune response, multiple lesions, and unstable immunity.

Aim

This study aims to analyze the clinicohistopathological correlation in different types of leprosy.

MATERIALS AND METHODS

This prospective study was conducted in the Department of Pathology, Coimbatore Medical College and Hospital, from January 2017 to October 2018. Inclusion criteria: Untreated leprosy patients were included in the study. Exclusion criteria: Patients who were on treatment for leprosy were excluded from the study. Histopathological study of skin biopsy specimens from clinically suspected leprosy patients was done. A detailed clinical history, examination findings indicating signs and symptoms of the skin lesions, and provisional clinical diagnosis were collected. Skin punch biopsies measuring 0.5 cm × 0.5 cm from the representative lesion were taken by the dermatologists and dispatched in plastic containers containing 10% formalin solution. Following fixation for 12–24 h, the tissues were processed embedded in paraffin and serial sections of 4–5 microns were obtained, which were stained with hematoxylin and eosin for morphological assessment and with fite faraco (FF) for identification of the bacilli. After studying the histopathological features and noting the bacteriological status, the diagnosis of leprosy was confirmed and classified according to Ridley and Jopling classification. H and E stained sections were studied to observe the various changes that occurred in the epidermis, papillary, reticular, deep dermis, neurovascular bundles, and adnexa. In addition, modified Fite FF stained sections were also studied to demonstrate lepra bacilli and the findings correlated with clinicohistopathological subtyping.

RESULTS

In this study, 162 patients who were clinically suspected as leprosy were included. The age of the study patients was range between 12 and 72 years; the incidence of leprosy was higher in the age group between 21 and 30 years. Male cases were higher in this study; the ratio was 1.6:1. In a histopathological examination of 162 cases, 154 cases were confirmed as leprosy.

A higher number of cases were reported in LL leprosy 41 cases (26.6%) followed by borderline lepromatous (BL) leprosy 39 cases (25.3%) [Figure 1].

The most common clinical features noted in this study was a loss of sensation, 90% of cases were reported and 65% of cases noted with nerve thickening, 60% with hypopigmented skin lesions.

The overall clinicohistopathological correlation was observed in 103 (68.6%) cases. Maximum concordance was seen in HL and ENL (100%), followed by TT (77.8%), BL (62.1%), borderline tuberculoid (BT) (62.1%), and LL (58%). It was least in MB (20%) [Table 2].

In histopathologically confirmed leprosy cases, 103 cases (67.6%) were positive in FF stain. All cases of HL and IL and most of the cases of LL, BL, and ENL showed the presence of FF stain positive lepra bacilli [Figure 2]. The bacillary index was high (+5 or +6) in these cases. Half of the cases of MB and few cases of BT also showed F.F. positivity with a low bacillary index ranging from +1 to +4. None of the cases of TT leprosy showed F.F. positivity.

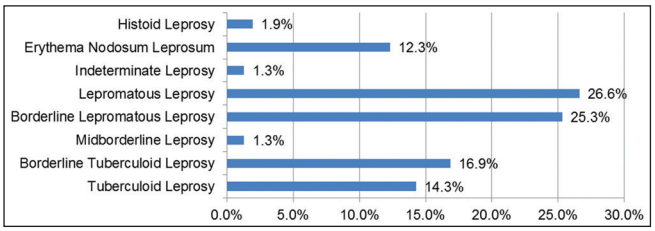

Figure 1: Distribution of cases of leprosy on histopathological examination

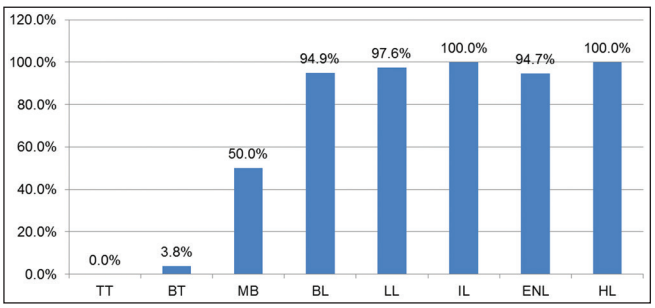

Figure 2: Distribution of Fite-Faraco stain positivity among various types of leprosy

Table 1: Cross-tabulation of clinical and histopathological classification in leprosy cases

Type	Clinically diagnosed	Histopathological classification									Percentage of parity
		TT	BT	MB	BL	LL	IL	ENL	HL	No evidence	
TT	18	14	1	0	0	0	0	0	0	3	77.8
BT	29	6	18	0	2	1	0	0	0	2	62.1
MB	5	0	2	1	2	0	0	0	0	0	20.0
BL	29	3	2	1	18	2	1	1	1	0	62.1
LL	69	2	4	0	14	40	1	4	0	4	58.0
IL	0	-	-	-	-	-	-	-	-	-	
ENL	11	0	0	0	0	0	0	11	0	0	100.0
HL	1	0	0	0	0	0	0	0	1	0	100.0

TT: Tuberculoid, BT: Borderline tuberculoid, BL: Borderline lepromatous, LL: Lepromatous

Table 2: Comparison of the spectrum of leprosy

Type	Present study (%)	Tiwari *et al.*[9] (%)	Kumar *et al.*[10] (%)	Nadia *et al.*[11] (%)
TT	14.3	7.5	18.9	14.4
BT	16.9	41.5	9.4	34.7
MB	1.3	0.0	0.0	0.0
BB	0.0	5.7	25.0	16.1
BL	25.3	15.0	7.0	5.9
LL	26.6	3.8	9.9	21.1
IL	1.3	26.4	8.0	4.2
ENL	12.3	0.0	17.9	0.0
HL	1.9	0.0	3.5	3.4

TT: Tuberculoid, BT: Borderline tuberculoid, BL: Borderline lepromatous, LL: Lepromatous

DISCUSSION

The correct classification of leprosy cases is an important tool for the proper allocation of patients in the multidrug therapy program since the duration of treatment and dosage of medication used differ between the paucibacillary and multibacillary forms.[7] Accordingly, evaluation of the agreement between classification systems using clinical criteria and those based on laboratory tests have been a frequent focus of studies over the past few years,[8] especially since the publication of the WHO operational classification, which recommends that the sole criterion for classifying patients should be the number of skin lesions, with allocation into two different therapeutic regimens.[7] Studies have shown that the use of this classification method alone, in routine practice within health-care services, presents limitations and different percentages of sensitivity and specificity [Table 2].[9,10] In the present study, the most common type of leprosy was the LL leprosy (26.6%) followed by BL leprosy (25.3%) while in other studies, TT or BT was more common.[11-13]

The inflammatory cells present in leprosy lesions are epithelioid cells, macrophages, lymphocytes, plasma cells, and in specific cases also neutrophils and mast cells.[14] According to the cell-mediated immune response to *M. leprae*, different types of granulomatous reaction can be observed. Epithelioid cells are usually seen in TT and BT, whereas foamy macrophages characterize the infiltrate of BL and LL. The infiltrate can often "touch" the epidermis in TT, but only rarely in BT and typically spares the epidermis in midborderline (BB), BL, and LL. Rarely, the infiltrate may be found in the superficial dermis only; more usually, it involves all the dermis and sometimes also the subcutis. Some cases may be characterized by a prominent lymphocytic infiltrate, resulting in a diagnostic pitfall. In each biopsy, the nerves have to be carefully checked. The presence of AFB inside the nerve is diagnostic of leprosy. Although the polar forms TT and LL are quite easily diagnosed and classified, borderline cases may sometimes present overlapping features. For this reason, combinations of symbols, such as TT-BT, BT-BB, BB-BL, and BL-LL, are used for those cases that show intermediate features among two groups.[14,15]

CONCLUSION

LL leprosy was more common in the region. Late diagnosis leads to continued transmission and increased risk of disability. Factors associated with late diagnosis include delay by patients in presenting and delay by health services in making a diagnosis.

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