Volume : 4 | Issue : 10 | October 2015 • ISSN No 2277 - 8179

Research Paper

Clinico - Histopathological Correlation in Leprosy: A Tertiary Care Hospital Based Study At Udaipur.

Medical Science

KEYWORDS : Leprosy, Histopathology, Ridley-Jopling Classification.

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ABSTRACT

Background and Objectives: *Leprosy is a chronic, infectious disease caused by Mycobacterium leprae, affecting mainly cutaneous and peripheral nervous system. Histopathology is an important tool to diagnose leprosy in situations where it mimics other clinical conditions. This study was conducted to know the correlation between clinical and histopathological diagnosis of leprosy.*

Methods: *Sixty cases were included over a period of 18 months, in whom leprosy was clinically diagnosed or suspected and biopsies were sent for histopathological confirmation. Histopathological findings are graded according to Ridley and Jopling scale. Clinicopathologic correlation was done along with Fite-Faraco stain.*

Results: *41(68.3%) were males and 19(31.60%) were females. Most common clinical feature was loss of sensation. Most common histological type was Borderline Tuberculoid seen in 22(36.66%) cases followed by Borderline Lepromatous 18(30%) cases, Tuberculoid 10(16.66%), Lepromatous Leprosy 4(6.66%), Histoid 2(3.33%) and Borderline Borderline 1(1.66%). Majority (58.3%) of cases were paucibacillary type and rests (41.6%) were of multibacillary type. Fite-Faraco staining was positive in 25(41.66%) cases. Clinico-histopathological correlation was observed in 41(68.3%) cases.*

Conclusions: *This study emphasis on correlation of clinical and histopathological features along with bacterial index to be more useful than considering any of the single parameters alone for accurate diagnosis of leprosy.*

Introduction

Leprosy, Hansen's disease is a chronic infectious disease caused by Mycobacterium Leprae principally affecting skin and peripheral nerves; it also involves muscles, eyes, bones, testis and internal organs.[1] The clinical manifestations are varied ranging from an insignificant skin lesion to extensive disease causing profound disability/deformities.[2] Depending on degree of immunity, clinical and histopathological features, various types of leprosy gradually may develop.[3] The mode of transmission is still unknown, but it is believed to be through inhalation of bacilli that are excreted from the nasal passages of the multibacillary patient.

Examination of a biopsy specimen for histopathology can be a valuable aid to reach confirmatory diagnosis and its subtypes, differential diagnosis and prognosis of the disease and assessment or regression of the disease in patient under treatment and also for research.[4,5]

Ridley & Jopling have proposed the classification of leprosy into five groups as Tuberculoid (TT), Borderline tuberculoid (BT), Mid-borderline (BB), Borderline lepromatous (BL) and Lepromatous (LL); with strict criteria for definition, this system has become generally accepted worldwide and is recommended.[6]

Present study has been conducted to know the histopathological features of leprosy in skin biopsies, to categorize these lesions into various types based on microscopy, bacillary index and to correlate with clinical presentations.

Materials and Methods

This is a hospital based study of 60 cases conducted at Department of Pathology, in a tertiary care hospital over a period of 18 months from August 2013 to December 2014. All patients with different clinical spectrum of leprosy, were included in the study and graded as per the Ridley-Jopling classification into TT, BT, BB, BL and LL. Punch biopsies were taken from active lesion and processed as per standard protocol. They were stained by Hematoxylin & Eosin stain and Fite-Faraco stain for identification of Mycobacterium leprae. Clinico-histopathological correlation was done.

Results

Total of 60 skin biopsies were histopathologically reported as leprosy during the 18 months study period. The age distribution of patients varied between 9-74 years, majority were between the age groups of 21-30 years followed by 31-40 years. Regarding gender distribution, 41(68.3%) were males and 19(31.6%) females with male to female ratio of 2.1:1. Clinically, 25(41.6%) cases showed loss of sensation, 16(26.6%) hypopigmented skin lesions, 11(18.3%) nerve thickening, 4(6.66%) erythematous skin lesions, 2(3.33%) nodules & 2(3.33%) trophic ulcers.

Among 60 cases, 41(68.3%) cases showed good correlation between clinical and histopathological diagnosis. Maximum correlation was observed in Borderline lepromatous (90.0%) followed by Borderline tuberculoid leprosy (84.6%). A poor correlation was seen in Tuberculoid leprosy (42.1%) (Table 1).

Table 1: Clinico histopathological Correlation

Clinical diagnosis	No. of pt.	TT	BT	BB	BL	LL	HL	IL	Agreement	%
TT	19	8	10	-	-	-	-	1	8/19	42.1
BT	13	2	11	-	-			-	11/13	84.6
BB	0	-	-	-	-	-	-	-	0	-
BL	20	-	-	1	18	-	-	1	18/20	90
LL	3	-	-	-	-	2	1	-	2/3	66.6
HL	2	-	-	-	-	1	1	-	1/2	50
IL	3	-	1	-	-	1	-	1	1/3	33.3
Total	60	10	22	1	18	4	2	3	41/60	68.3

Most common clinical type of leprosy was tuberculoid group of leprosy. Tuberculoid and Borderline tuberculoid leprosy constituted 19(31.6%) and 13(21.6%) cases respectively. Borderline lepromatous and Lepromatous Leprosy constituted 20(33.3%) and 3(5%) cases respectively.

Most common histological type of leprosy was Borderline Tuberculoid leprosy seen in 22(36.6%) cases followed by Borderline Lepromatous seen in 18(30.0%) cases. Histopathologically, epidermal and dermal changes are summarized in Table 2. Most of cases were paucibacillary 35(58.3%) and 25(41.6%) multibacillary. All tuberculoid leprosy and indeterminate leprosy were neg-

Volume : 4 | Issue : 10 | October 2015 • ISSN No 2277 - 8179

ative in Fite-Faraco stain.

Table 2: Histopathological Changes observed in Epidermis and Dermis in Leprosy

Epidermal change								
	TT (10)	BT (22)	BB (1)	BL (18)	LL (4)	HL (2)	IL (3)	Total (60)
Atrophy/Thinning	4	7	1	15	4	2	1	34 (56.6%)
Ulceration/Erosion	4	9	-	2	-	-	-	15 (25.0%)
Unremarkable	2	6	-	1	-	-	2	11 (18.3%)
Dermal change								
Epithelioid granuloma	8	12	1	-	-	-	-	21 (35%)
Giant cell	5	2	-	-	-	-	-	7 (11.6%)
Periappendageal lymphocyte	-	8	-	1	-	1	-	10 (16.6%)
Perivascular lymphocyte	1	7	-	2	1	2	-	13 (21.6%)
Perineural lymphocyte	1	7	-	3	-	1	-	12 (20%)
Macrophages	1	2	1	16	4	1	3	27 (45%)
Grenz zone	-	9	1	15	4	1	3	32 (53.3%)

Discussion

Leprosy is a slowly progressive infection caused by Mycobacterium leprae affecting the skin and peripheral nerves. In the present study, Ridley-Jopling classification was used to classify leprosy histopathologically in all cases. Indeterminate and histoid types of leprosy were also included for analysis. Histopathological examination of skin lesion is the gold standard for accurate diagnosis.[7]

Leprosy can occur at all ages.[8] In the present study, patients of 20-29 years were affected most and patients below 9 years were affected least. Similar observations were made by Guha et al [9], Sehgal et al [10], Murthy et al [11] and Kaur I et al [12]. Variable and long incubation period may be responsible for this age distribution.[11] Generally, leprosy is believed to be commoner in males.[1,13] This is observed in studies by Sehgal et al [10], Nadkarni et al [14], and Murthy et al [11] etc. In this study, male predilection was seen in 68.3% of cases.

There was complete agreement between the clinical and histopathologic diagnosis in 68.3% of the cases. Different studies have been performed regarding clinico-histopathological correlation, and showed variable results. (Table 3)

Table 3: Comparative study in clinico-pathological correlation by different Studies.

Various studies	No. of cases	Clinico-histopathological correlation(%)
Present study(2014)	60	68.3
Pandya AN et al. (2008)	50	58
Murthy BN et al. (2001)	372	62.63
Kalla G et al. (2000)	736	64.7
Jerath VP et al. (1982)	130	68.5
Ridley DS et al. (1966)	82	68.3

In the present study, positive clinico-histopathological correlation was better noted in BT and BL group in comparison to TT. The most commonly encountered type of leprosy was BT (36.6%), followed by BL (30.0%). Borderline group constituted the major spectrum (68.33%), similar to findings of other authors like Murthy et al [11], Verma et al [15] & Shenoi et al [19].

COMPARISON OF CLINICAL FEATURES

Present study showed that loss of sensation was the commonest clinical feature followed by hypopigmented skin lesions and nerve thickening, trophic ulcer was rare. Similar observations were made by Verma et al.[15]

The following criteria were used for diagnosis of various types of Leprosy:

1) TT: Collections of epithelioid cells, many lymphocytes peripheral to the granuloma and/or several large Langhan's giant cells[16,17] or a very large granulomatous nerve with intact perineurium or caseation in a nerve centre or erosion of epidermis by epithelioid cells.
2) BT: Presence of epithelioid cell granuloma which was more diffuse than in TT[6] with few small giant cells and moderate number of lymphocytes often within the granuloma.[16]
3) BB: Features of both TT and LL present.[18]
4) IL: Mild non-specific perivascular and periadnexal lymphocytic and histiocytic infiltrate in dermis or thickened deep dermal nerve showing intraneural lymphocytic infiltration.[17] In IL, the histopathological changes are minimal and may be missed unless the biopsy is adequate, including the entire dermis and part of subcutis.[17]
5) BL: Diffuse infiltrates of macrophages, foamy macrophages and few lymphocytes seen involving nerves and appendages.[18]
6) LL: Diffuse infiltrate of macrophages and foamy cells, with few or no lymphocytes.[17, 18]

The different clinical form through which leprosy manifests is accompanied by specific histopathological picture. Thus towards TT end of the spectrum, histopathology shows

epithelioid cells, Langhan's giant cells and lymphocytes and while towards LL end of spectrum, there are more foamy macrophages.[24]

TT is slightly different from BT leprosy, both clinically and histopathologically. The line of demarcation often overlaps. Many cases diagnosed clinically as TT have histological evidence of BT.[20]

Separation of BL from LLs is very difficult [21], while diagnosing LL, clinical features were also correlated along with strict criteria of paucity in lymphocytes.

Indeterminate leprosy cases appear to be problematic due to the non specific histology of their lesions, variable factors such as nature and depth of biopsy, the quality of section and number of acid fast stained sections examined etc. and inter-observer variations, both clinically and histopathologically.[20]

Nervous system plays an important role in modulation of the inflammatory response. In areas where modulation has favorably affected the host defense and repair mechanisms, no evidence of disease results. In other areas with different grades of modulation affecting the host defense response unfavorably, different types of clinicopathological pictures are seen. This concept explains the disagreement in clinical and histopathological classification observed in some cases of leprosy.[22]

BACILLARY INDEX

It was highest in LL types and low in BT types. Jopling also observed that the bacilli are scanty or absent in BT, always present in BB and numerous in BL and LL.[6] It also shows the variation of cell mediated immunity and bacillary load as the spectrum of leprosy moves from tuberculoid pole to lepromatous pole. The present study confirms the same.

In paucibacillary leprosy IL, TT, BT are included while BB, BL, LL and histoid are considered as multibacillary type of leprosy based on technical report of WHO study group 1982.[25] WHO expert committee (1988)[26] made a change that paucibacillary type should include only smear negative IL, TT, BT cases and any case belonging to these types with smear positivity is classified as Multibacillary leprosy for purpose of multidrug therapy.

Clinical information like site of lesion, type of lesion, nerve involvement, sensory impairment, treatment history along with immunological status of patients is very important for the pathologist to correlate histopathologically. Histopathological diagnosis also depends on various factors like size of biopsy specimen, age of lesion, depth of biopsy, quality of section and very important interobserver variation has a role in clinico-pathological evaluation.[23]

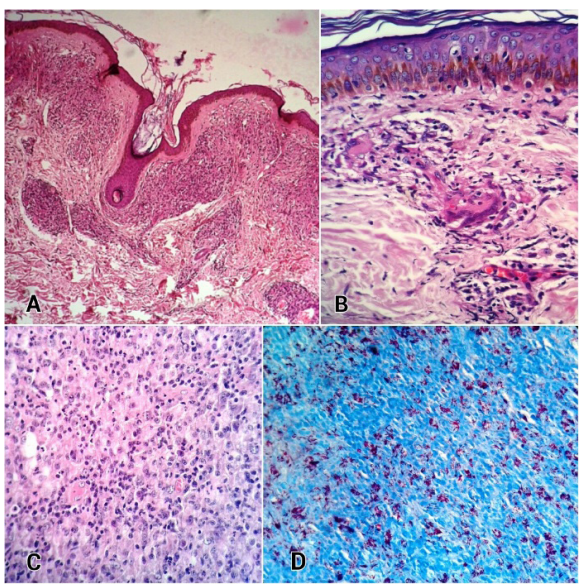

Figure 1
A) BL - Grenz Zone and Epitheliod granuloma
B) TT - Epitheliod granuloma with langhans giant cell
C) Histoid Leprosy
D) Fite-Faraco stain of Histoid Leprosy - BI +6

Conclusion

As there can be some degree of overlapping among different types of leprosy both clinically and histopathologically, the present study emphasizes on clinico-histopathological correlation along with bacteriological index than considering any of the single parameters alone for accurate diagnosis of Leprosy. However, the sample size was small, as the study was conducted in a short duration. Therefore, the results cannot be extrapolated.

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