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Original Research Article

A clinicopathological study of leprosy: a study of skin biopsies

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ABSTRACT

Background: Leprosy is a chronic infectious granulomatous disease caused by *Mycobacterium leprae*. The disease mainly affects peripheral nervous system, the skin and other tissues such as the muscles, bones and joints, eyes, reticuloendothelial system, testis etc. To reduce global load of leprosy, it is essential to have an early and proper diagnosis by clinical and histopathological correlation followed by proper and complete treatment. Aims and Objectives were 1) to study histopathological spectrum of various subtypes of leprosy, 2) to study the age and gender wise incidence of different subtypes of leprosy, and 3) to assess the concordance between clinical and histological diagnosis in cases of leprosy using Ridley-Jopling scale.
Methods: A retrospective observational study of 126 skin biopsies diagnosed as leprosy over a period of one year from August 2020 to July 2021 at P. D.U. Medical College and Hospital, Rajkot, Gujarat.
Results: In this study, most of cases occurred in age group (21-40) years (50.8%) and showed marked male predominance with M:F ratio=2.7:1. Lepromatous leprosy (40.5%) was the most common histopathological type of leprosy. Maximum clinicopathological correlation seen in HL (100%), LL (90%) and TT (71.4%).
Conclusions: Histopathological examination of skin biopsies and clinicopathological correlation both are essential for early and accurate diagnosis and typing of leprosy which is helpful in prevention of deformities and drug resistance by early and appropriate treatment.

Keywords: Clinicopathological correlation, Leprosy, Modified FF stain, Skin biopsy

INTRODUCTION

Leprosy is a chronic infectious granulomatous disease caused by *Mycobacterium leprae*.[1] Leprosy (Hansen's disease) was discovered by Sir Gerhard Armauer Hansen in 1873.[2] Although, leprosy had already been described in Susruth Samhita (600 BC).[3] It can affect any age group and both gender.[4] The disease mainly affects peripheral nervous system, the skin and other tissues such as the muscles, bones and joints, eyes, reticuloendothelial system, testis etc.[5] '*Mycobacterium leprae*' organism cannot be cultured.[6] So, diagnosis of leprosy depends on microscopy and demonstration of Acid Fast Bacilli (AFB) on tissue biopsy.[7,8] Clinical and histopathological presentation of leprosy depends on the host cellular immune response.[9] According to Ridley-Jopling classification, leprosy is classified into 5 groups: tuberculoid (TT), borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL), lepromatous (LL) (Table 1).[10] Histopathological characteristics of various types of leprosy shown in (Table 2).[11] India has 60% of the entire global case load of leprosy.[12] In 2016 WHO has launched the global leprosy strategy 2016-2020: "Accelerates towards a leprosy free world." It aims to do efforts for leprosy control and to avoid disability, especially among children affected by the disease in endemic countries.[13] Global load of leprosy can be reduced by proper and complete treatment of various subtype of leprosy. It is essential to have an early and proper diagnosis by clinical and histopathological correlation.

Table 1: Clinical aspects of Ridley-Jopling classification of leprosy.

Observation or test	Type of leprosy				
	TT	BT	BB	BL	LL
Number of lesions	Single usually	Single or few	Several	Many	Very many
Size of lesions	Variable	Variable	Variable	Variable	Small
Surface of lesions	Very dry, sometimes scaly	Dry	Slightly shiny	Shiny	Shiny
Sensation in lesions (not face)	Absent	Moderately or markedly diminished	Slightly or moderately diminished	Slightly diminished	Not affected or minimally affected
Hair growth in lesions	Absent	Markedly diminished	Moderately diminished	Slightly diminished	Not affected
AFB in lesions	Nil	Nil or scanty	Moderate numbers	Many	Very many (plus globi)
AFB in nasal scraping or in nose blows	Nil	NIL	Nil	Usually nil	Very many (plus globi)
Lepromin test	Strongly positive (+++)	Weakly positive (+ or ++)	Negative	Negative	Negative

[Acidfast bacilli (AFB), Tuberculoid (TT), Borderline tuberculoid (BT), Mid-borderline (BB), Borderline lepromatous (BL), Lepromatous (LL)] (+ - Positive).

Table 2: Histopathological characteristics of various types of leprosy.

Types parameter	IL	TT	BT	BB	BL	LL
Granuloma	Absent	Epitheloid cells	Epitheloid cells	Mixed cellular	Macrophages	Macrophages
T-lymphocytes	4+	4+	3+	2+	2+	1+
Epitheloid cells	Absent	4+	3+	2+	1+	Absent
Giant cells	Absent	3+	4+	Absent	Absent	Absent
Macrophage	Absent	Absent	1+	2+	3+	4+
Bacterial index	Negative	Negative	1+	2-3+	3-4+	5-6+

[Intermediate Leprosy (IL), Tuberculoid (TT), Borderline tuberculoid (BT), Mid-borderline (BB), Borderline lepromatous (BL), Lepromatous (LL)] (+ - Positive).

Aims and objectives

Primary objective was to study histopathological spectrum of various subtypes of leprosy. Secondary objectives were to study the age and gender wise incidence of different subtypes of leprosy and to assess the concordance between clinical and histological diagnosis in cases of leprosy using Ridley-Jopling scale

METHODS

Study design

It was a retrospective observational study.

Study population, study period and study site

All 126 skin biopsies diagnosed as leprosy over a period of one year (August 2020 to July 2021) at department of Pathology, P. D. U. hospital, Rajkot, Gujarat were included in this study.

Inclusion criteria

Skin biopsies with provisional diagnosis or differential diagnosis of leprosy from skin department irrespective of age and gender of the patient were included.

Exclusion criteria

Those cases where leprosy was suspected clinically but not confirmed on biopsies were excluded from the study.

Processing of biopsy specimen

After receiving, skin biopsies were fixed in 10% neutral buffered formalin and submitted to routine tissue processing and paraffin embedding. Sections of 5 µ thickness were made, slides were stained by Hematoxylin-Eosin (H and E) and modified Fite-Faraco's stain (FF) and slides were examined under light microscope. Ridley-Jopling criteria were used to classify the disease histopathologically and clinically.

Ethical considerations

The study was approved by the institutional review board and the ethics committee of P. D. U. Medical College and Hospital, Rajkot with reference number 94/2021.

Statistical analysis

Statistical analysis was done after collecting the primary data. Data was entered in Microsoft excel and analysis was done in the form of percentages and proportions and it was represented in tables.

RESULTS

In this study, most of cases occurred in the age group of (21-40) years (64 cases, 50.8%) followed by age group (41-60) years (28 cases, 22.2%) and the minimum incidence seen in the age group (61-80) years (16 cases, 12.7%).

Table 3: Age and gender wise distribution of various type of leprosy.

Histopathological type	TT		BT		BB		BL		LL		LL with ENL		HL		Total		Total
Age (years)	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	
1-20	4	0	2	0	2	0	2	1	2	2	0	1	2	0	14	4	18
21-40	4	2	1	4	6	1	7	3	21	7	3	1	4	0	46	18	64
41-60	1	1	0	1	2	1	3	0	9	2	0	2	4	2	19	9	28
61-80	1	0	1	3	2	0	0	0	8	0	0	0	1	0	13	3	16
Total	10	3	4	8	12	2	12	4	40	11	3	4	11	2	92	34	126
Total	13		12		14		16		51		7		13		126		

[Tuberculoid (TT), Borderline tuberculoid (BT), Mid-borderline (BB), Borderline lepromatous (BL), Lepromatous (LL), Histoid (HL), Lepromatous leprosy with Erythema nodosum leprosum (LL with ENL)].

Table 4: Clinical features.

Clinical Features	Type	TT	BT	BB	BL	LL	HL	Total
	No.	13	12	14	16	58	13	126
Hypopigmented patches		13 (100%)	10 (83.3%)	12 (85.7%)	14 (87.5%)	45 (77.6%)	10 (69.2%)	104 (82.5%)
Erythematous patches		0	5 (41.7%)	0	5 (31.3%)	15 (25.9%)	4 (30.8%)	29 (23%)
Combined (macules and papules)		0	1 (8.3%)	4 (28.6%)	5 (31.25%)	13 (22.5%)	3 (23.1%)	26 (20.1%)
Anesthesia (loss of sensation)		13 (100%)	11 (91.2%)	9 (64.3%)	16 (100%)	51 (88%)	10 (69.2%)	110 (87.3%)
Nerve involvement		8 (61.5%)	4 (33.3%)	3 (21.4%)	9 (56.3%)	56 (96.5%)	10 (69.2%)	90 (71.4%)
Trophic ulcer		3 (23%)	2 (16.7%)	3 (21.4%)	3 (18.8%)	0	0	11 (8.7%)
Limb deformities		0	3 (25%)	0	4 (25%)	0	0	7 (5.6%)

[Tuberculoid (TT), Borderline tuberculoid (BT), Mid-borderline (BB), Borderline lepromatous (BL), Lepromatous (LL), Histoid (HL), Lepromatous leprosy with Erythema nodosum leprosum (LL with ENL)].

Table 5: Clinicopathological correlation.

Clinical diagnosis	Histopathological diagnosis						Total
	TT	BT	BB	BL	LL	HL	
TT	10	1	0	0	3	0	14
BT	3	8	1	1	2	0	15
BB	0	1	10	2	3	0	16
BL	0	2	2	10	5	0	19
LL	0	0	1	3	45	0	49
HL	0	0	0	0	0	13	13
Total	13	12	14	16	58	13	126
Agreement (%)	76.9%	66.7%	71.4%	62.5%	77.6%	100%	71.2%

[Tuberculoid (TT), Borderline tuberculoid (BT), Mid-borderline (BB), Borderline lepromatous (BL), Lepromatous (LL), Histoid (HL), Lepromatous leprosy with Erythema nodosum leprosum (LL with ENL)].

Out of total 126 cases, 92 cases (73%) were males and 34 cases (27%) were females with M:F ratio 2.7:1. Male predominance was seen in all types of leprosy.

In present study, most common type of leprosy was lepromatous leprosy (51 cases, 40.5%) followed by borderline lepromatous leprosy (16 cases, 12.7%), midborderline leprosy (14 cases, 11.1%), tuberculoid leprosy (13 cases, 10.3%), histoid leprosy (13 cases, 10.3%), borderline tuberculoid leprosy (12 cases, 9.5%), lepromatous leprosy with erythema nodosum leprosum (7 cases, 5.6%).

Table 6: Distribution (%) of FF stain positivity among various type of leprosy.

Type of leprosy	Total cases	No. of cases positive for FF stain (%)
LL	51	45 (88.2)
BL	16	11 (68.75)
BB	14	2 (14)
BT	12	0 (0)
TT	13	5 (38.5)
HL	13	13 (100)
LL with ENL	7	5 (71.4)

[Tuberculoid (TT), Borderline tuberculoid (BT), Mid-borderline (BB), Borderline lepromatous (BL), Lepromatous (LL), Histoid (HL), Lepromatous leprosy with Erythema nodosum leprosum (LL with ENL)]

According to this study, most common observed clinical feature was anesthesia (loss of sensation) (87.3%) followed by hypopigmented patches (82.5%), nerve involvement (71.4%), erythematous patches (23%), Combination of lesions (macules and papules) (20.1%), trophic ulcer (8.7%) and limb deformities (5.6%).

In this study, maximum clinicopathological correlation seen in histoid leprosy (100%) followed by lepromatous leprosy (77.6%), tuberculoid leprosy (76.9%), borderline leprosy (71.4%), borderline tuberculoid leprosy (66.7%) and borderline lepromatous leprosy (62.5%).

In this study, highest percentage of positivity of FF stain seen in HL (100%) followed by LL (88.2%), LL with ENL (71.4%), BL (68.75%), TT (38.5%), BB (14%) and BT (0%) (Table 6).

DISCUSSION

In this study, age of patient ranged from 8-76 years and most of cases occurred in age group (21-40) years (50.8%) which is comparable with Shivani et al, Ruchi et al and Boomakanti et al.[14,16,17] This study showed marked male predominance with M:F ratio = 2.7:1 which comparable with Shivani et al, Roy et al and Ruchi et al.[14-16] Anesthesia (loss of sensation) (87.3%) and hypopigmented patches (82.5%) were the most common clinical features observed in this study which is comparable with Roy et al and Khammankar et al.[15,18] In this study, highest percentage of positivity of FF stain seen in HL (100%) and LL (88.2%) while according to Ruchi et al highest percentage of positivity of FF stain in LL (100%) and BT (100%).[16]

Table 7: Comparison of spectrum of leprosy of present study with various studies.

Type	Present study	Shivani et al[14]	Roy et al[15]	Kumar et al[19]	Nadia et al[20]	Ruchi et al[16]
TT	10.3%	19.5%	16.0%	18.9%	14.4%	4.0%
BT	9.5%	14.6%	36.0%	9.4%	34.7%	14.0%
BB	11.1%	4.9%	0.0%	25.0%	16.1%	43.0%
BL	12.7%	4.9%	12.0%	7.0%	5.9%	17.0%
LL	40.5%	17.7%	8.0%	9.9%	21.1%	11.5%
IL	0.0%	9.8%	8.0%	8.0%	4.2%	5.5%
LL with ENL	5.6%	17.1%	8.0%	17.9%	0.0%	3.5%
HL	10.3%	4.9%	12.0%	3.5%	3.4%	1.5%

[Tuberculoid (TT), Borderline tuberculoid (BT), Mid-borderline (BB), Borderline lepromatous (BL), Lepromatous (LL), Histoid (HL), Lepromatous leprosy with Erythema nodosum leprosum (LL with ENL)]

Table 8: Comparison of clinicopathological correlation.

Studies	TT	BT	BB	BL	LL	HL
Present study	76.9%	66.7%	71.4%	62.5%	77.6%	100%
Sindhushree et al[21]	25%	37.89%	8.30%	12.50%	33.30%	57.14%
Kalla et al[22]	76.70%	44.20%	37%	43.70%	75.60%	_

[Tuberculoid (TT), Borderline tuberculoid (BT), Mid-borderline (BB), Borderline lepromatous (BL), Lepromatous (LL), Histoid (HL), Lepromatous leprosy with Erythema nodosum leprosum (LL with ENL)]

In this study, lepromatous leprosy (40.5%) and borderline lepromatous leprosy (12.7%) were the most common histopathological type of leprosy which was comparable with Khamankar et al but incidence of LL was much higher in comparison with Nadia et al (21.1%), Shivani et al (17.7%), Ruchi et al (11.5%), Kumar et al (9.9%) and Roy et al (8%).[14-16,18-20] This might be due to high infectivity of LL and increase occurrence of LL in Gujarat in comparison to other regions.

Different studies showed variable clinicopathological correlation. In present study, maximum clinicopathological correlation seen in cases of HL (100%) which was comparable with Sindhushree et al (57.14%) while in Kalla et al maximum clinicopathological seen in cases of TT (76.70%).[21,22]

CONCLUSION

Histopathological examination of skin biopsies and clinicopathological correlation both are essential for early and accurate diagnosis and typing of leprosy which is helpful in prevention of deformities and drug resistance by early and appropriate treatment.

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