Original Article

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Pathology Section

Clinico-pathological Study of Leprosy- A Descriptive Study

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ABSTRACT

Introduction: Leprosy is an age old disease affecting mankind with various clinico-pathological forms. *Mycobacterium Leprae* causes a chronic infectious disease known as Leprosy or Hansen's disease. It remained a major public health issue due to associated case load, morbidity and stigma attached to it. Clinical and histopathological examination along with demonstration of lepra bacilli in skin smears by Fite-faraco stain and Bacillary Index (BI) is widely used for proper classification and diagnosis of leprosy.

Aim: To study the clinico-pathological features of leprosy in skin biopsies and to categorise it into various types of lesions according to Ridley Jopling classification.

Materials and Methods: The descriptive study included clinically diagnosed 183 leprosy cases who underwent skin biopsy for histopathological examination from January 2017 to December 2018 at Shri Bhausaheb Hire Government Medical College Dhule, Maharashtra. All sections were stained with Haematoxylin and Eosin (H&E) and Fite-faraco stain. Ridley-Jopling classification was done to classify leprosy. Clinical diagnosis was in concordance with that of histopathological diagnosis.

Results: A total of 183 skin biopsies were studied from patients in an age group of 11-76 years. Male to female ratio was 1.5:1 and commonest age group affected was 21-40 years. Clinically, 78 cases (42.6%) were diagnosed as Borderline Tuberculoid (BT) leprosy followed by indeterminate leprosy 34 (18.57%). On histopathological examination maximum cases had BT leprosy 64 (82.05%) followed by Tuberculoid (TT) leprosy 13 (81.25%). Fite-faraco stain was done in 71 cases and was found positive in all cases of Borderline Lepromatous (BL) and Lepromatous Leprosy (LL). Also,concordance between Bacillary Index (BI) and histopathology examination was done. The clinico-histopathological concordance was seen in 127 cases (69.39%).

Conclusion: Early and accurate diagnosis by clinical and histopathological examination along with special stain is essential for proper diagnosis and treatment of the patient as well as prevention of its complications.

Keywords: Borderline tuberculoid leprosy, Clinico-histopathological examination, Fite-faraco stain

INTRODUCTION

Leprosy is a major public health problem in developing countries including India and it presents in different clinico-pathological forms depending on the immune status of the host [1]. Leprosy is a chronic granulomatous inflammation caused by *Mycobacterium leprae* and commonly affects skin, nerves and also involves muscles, eyes, bone, testis and internal organs. Various clinical manifestations are seen ranging from an insignificant skin lesion to extensive disease causing significant disabilities and deformities [2].

In India, the overall prevalence of leprosy has decreased from 5.27/10000 in the year 2000 to 0.67/10000 in the year 2018. Despite of all advances in medical science leprosy continues to be a public health challenge [3]. 60% of newly reported cases per year across the globe are from India warranting a sustainable effort to reduce the numbers [4]. WHO launched a five year "Global leprosy strategy 2016-2020' in April 2016 tilted 'Accelerating towards a leprosy-free world" [5].

In 1960, Ridley and Jopling classified leprosy based on immunological aspects into five types: Tuberculoid (TT), Borderline Tuberculoid (BT), Mid Borderline (BB), Borderline Lepromatous (BL) and Lepromatous Leprosy (LL) [6]. It is further subdivided according to the number of acid-fast bacilli present in the dermis, which is expressed on a logarithmic scale by the Bacteriological Index (BI) [7]. In 1982, WHO recommended categorisation into Paucibacillary (PB) and Multibacillary (MB) based on skin lesions and/or nerve trunk involvement (PB leprosy <5 lesions; MB leprosy >5 lesions) [8].

Diagnosis of leprosy is based on clinical examination, demonstration of acid fast bacilli in skin smears by Fite-faraco stain and histopathological examination [9].

Due to clinical diversity, leprosy is sometimes difficult to diagnose clinically. Histopathological examination of skin biopsies provides a valuable aid to arrive at confirmatory diagnosis and its exact typing, correct and adequate treatment and progression and regression of disease in patients under treatment. So, clinico-pathological correlation in leprosy assumes a greater significance [10]. The objective of this study was to categorise skin biopsies of leprosy into various subtypes on histopathological examination and to estimate the concordance between clinical and histopathological diagnosis in cases of leprosy using Ridley-Jopling classification.

MATERIALS AND METHODS

The present descriptive study was conducted in Department of Pathology Shri Bhausaheb Hire Government Medical College, Dhule, Maharashtra, India over a period of two years from January 2017-December 2018. During the study period, total 428 skin biopsies were received in histopathology section in Department of Pathology. Institutional Ethical Committee approval was taken wide Ref no. 19 IEC/ACPMMC/Dhule. Among these 183 skin biopsies were clinically diagnosed as leprosy.

Inclusion criteria: Newly diagnosed leprosy patients with hypopigmented patches with loss of sensation were included in the study.

Exclusion criteria: Patient who had taken antileprosy treatment in past, patient who was on anti-leprosy treatment and inadequate biopsy sample were excluded from the study.

Biopsies which lacked the full depth of dermis along with a portion of subcutaneous fat were considered as inadequate. Detailed clinical history like age, sex and clinical diagnosis was noted. Skin biopsies were performed by the Dermatologist and were sent to

the Department of Pathology in 10% formalin. After adequate fixation, the biopsies were submitted for routine processing, followed by paraffin embedding and sectioning. All sections were stained with H&E and Fite-faraco stain to demonstrate acid fast bacilli. The cases were classified according to Ridley Jopling classification [6]. The histopathological slides, Fite-faraco slides and BI were reviewed.

STATISTICAL ANALYSIS

The data was collected and entered into Microsoft excel spread sheet and percentages were calculated.

RESULTS

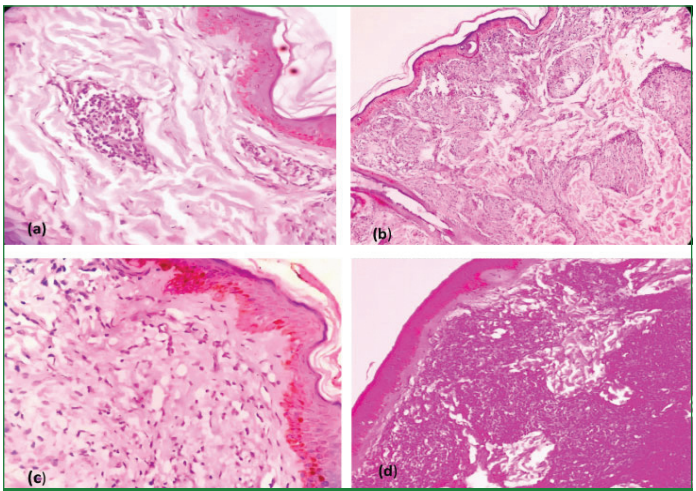
The present study included 183 skin biopsies were clinically diagnosed as leprosy. Age group of patients ranged from 11 years to 76 years. Majority of patients 86 (46.99%) were in the age group of 21 to 40 years followed by 52 (28.41%) in 41 to 60 years [Table/Fig-1].

Age group in years	Number of cases	Percentage (%)
Below 20	10	5.46
21-40	86	46.99
41-60	52	28.41
61-76	35	19.13
Total	183	100

[Table/Fig-1]: Age wise distribution of cases.

There were 112 (61.20%) male patients and 71 (38.79%) female patients, with male to female ratio (M:F) of 1.5:1. Most of the patients presented with hypopigmented patch i.e 118 (64.48%) cases followed by erythematous macule, papule and nodule. Clinically, maximum 78 (42.6%) cases were diagnosed as BT leprosy followed by indeterminate leprosy 34 cases (18.57%), LL 19 (10.38%), TT leprosy 16 (8.74%), BL leprosy 25 (13.66%), and 6 (7.22%) cases of histoid leprosy.

On histopathological examination, the most common type was BT leprosy in 64 cases followed by indeterminate leprosy in 16 cases, LL in 12 cases, BL leprosy in 16 cases and TT leprosy in 13 cases. Out of the six cases of clinically diagnosed histoid leprosy, four cases were confirmed as histoid leprosy and two cases were LL histopathologically. On histopathological examination, one case showed features of histoid leprosy and erythema nodosum leprosum which were clinically diagnosed as LL [Table/Fig-2 (a-d)].



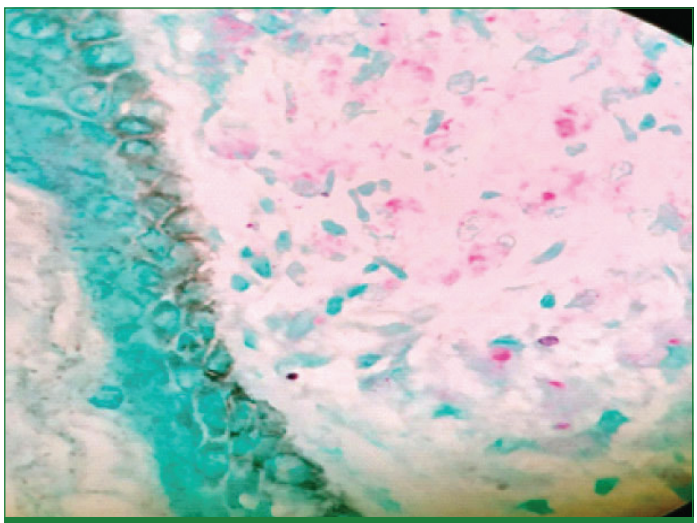
[Table/Fig-2]: Photomicrograph showing: (a) Borderline Tuberculoid (BT) leprosy showing granuloma of epitheloid cells and lymphocytes in dermis (H&E x400); b) Tuberculoid (TT) leprosy showing epitheloid cell granulomas eroding the basal layer of epidermis (Haematoxylin and Eosinx100); (c) Lepromatous Leprosy (LL) showing grenz zone with foamy macrophages in dermis (H&E x400); (d) histoid leprosy showing interlacing bands of spindle cells. (Haematoxylin and Eosin x100).

Overall concordance of histopathological diagnosis with clinical diagnosis was seen in 127 cases (69.39%). The clinico-histopathological concordance was highest in BT leprosy [Table/Fig-3].

Clinical diagnosis	Histopathological diagnosis								Others
	TT	BT	BB	BL	LL	IL	ENL	Histoid	
TT (16)	13	2	-	-	-	1	-	-	0
BT (78)	4	64	-	2	-	2	-	-	6
BB (5)	-	-	2	-	-	-	-	-	3
BL (25)	-	2	-	16	2	-	-	-	5
LL (19)	1	1	-	3	12	-	1	1	0
IL (34)	-	5	-	2	-	16	-	-	11
Histoid (6)	-	-	-	-	2	-	-	4	0
Total: 183	18	74	2	23	16	19	1	5	25

[Table/Fig-3]: Clinico-histopathological concordance.
TT: Tuberculoid leprosy; BT: Borderline leprosy; BB: Midborderline leprosy; BL: Borderline lepromatous leprosy; LL: Lepromatous leprosy; IL: Indeterminate leprosy

In our study, 25 cases were not diagnosed as leprosy. So Fite-faraco staining was done in 158 cases. Out of 158 cases, 71 (44.93%) were found positive for Fite-faraco stain. No acid fast bacilli could be demonstrated in cases of TT leprosy and BB leprosy. All histologically diagnosed cases of BL leprosy, LL and histoid leprosy showed positivity for lepra bacilli. Twenty five cases of BT leprosy and two cases of indeterminate leprosy showed positivity for lepra bacilli [Table/Fig-4].



[Table/Fig-4]: Fite farraco stain: positive for Acid fast bacilli (100X).

Based on the Ridley and Jopling logarithmic scale, BI was studied in 158 Fite-faraco stained slides and observed positive in 71 cases. BI observed was 0 (zero) in case of TT and 5+/6+ in cases of LL and its variant of histoid leprosy [Table/Fig-5]. Indeterminate leprosy is not included in Ridley Jopling classification system due to lack of distinguishing features.

BI (21)	IL (19)	TT (18)	BT (74)	BB (2)	BL (23)	LL (16)	HISTOID (5)	ENL (1)	Total
0	0	0	0	0	0	0	0	0	0
1+	2	0	18	0	0	0	0	0	20
2+	0	0	7	0	0	0	0	0	7
3+	0	0	0	0	8	0	0	0	8
4+	0	0	0	0	11	4	0	0	15
5+	0	0	0	0	4	9	0	0	13
6+	0	0	0	0	0	3	5	0	8

[Table/Fig-5]: Bacillary Index (BI) with histopathological concordance.
BI: Bacillary index; TT: Tuberculoid leprosy; BT: Borderline leprosy; BB: Midborderline leprosy; BL: Borderline lepromatous leprosy; LL: Lepromatous leprosy; IL: Indeterminate leprosy, ENL: Erythema nodosum leprosum

DISCUSSION

Leprosy is one of the oldest diseases known to man. It is a chronic contagious disease with various clinical presentations, which can mimic many diseases other than leprosy. A definitive diagnosis of leprosy cases cannot be reached based on clinical examination alone; thus the diagnostic accuracy is enhanced through the histopathological examination [6]. So, histopathological examination continues to be an important tool in accurate diagnosis and classification of leprosy and still remains the gold standard. During the study period of two years 183 skin biopsies were clinically diagnosed as leprosy.

In present study majority of cases were male (61.20%) and the male to female ratio was (1.5:1). These findings were correlated with the findings of other studies [11-13]. The possible cause of male predominance of leprosy is considered to be environmental, more chances of contact, urbanisation and industrialisation. Leprosy can be seen in any age. In present study maximum cases were in 21-40 years of age group. Majority of the studies showed maximum cases in the same age group [12,14]. In our study, least number of cases (5.46%) were reported below the age of 20 years. This may be due to longer incubation period of lepra bacilli [15]. The eldest case in our study was a 72-year-old while a 11-year-old boy was the youngest case. Most of the patients presented with hypopigmentedpatch (64.48%) and the remaining with erythematous macule and papule. Similar studies were seen in some other studies also [13,14,16]. Vahini G et al., observed 56% cases of hypopigmented plaque with loss of sensation [17].

In the present study, the majority of the patients were found to be in the borderline spectrum of leprosy. Similar findings were seen by Shivamurthy V et al., and Banushree CS et al., [13,18]. In our study clinically and histopathologically, the most common diagnosis was BT leprosy which is in concordance with Tiwati M et al., Shivamurthy V et al., and Bal A et al., [12,13,19]. In a recent study of Semwal S et al., Vahini G and Hazarika D et al., also reported the maximum cases of BT leprosy [11,17,20].

Histopathologically, in TT leprosy well formed epitheloid cell granuloma with a rim of lymphocytes distributed throughtout the dermis and enroaching the basal layer of the epidermis were seen. In BT leprosy, granulomas have a fewer number of lymphocytes and more giant cells and epidermal erosion will not be seen. Erosion into the epidermis with absence of grenz zone when present is a useful feature in differentiating TT leprosy and BT leprosy. In BL leprosy, the lymphocytes are more prominent and there is a tendency for some activation of macrophages to form poorly to moderately defined granulomas. Perineural fibroblast proliferation forming an 'onion skin' is typical. Foamy cells are not prominent and LL diffuse sheets of foamy histiocytes with grenz zone [21].

Indeterminate leprosy is not included in Ridley Jopling classification system due to lack of distinguishing features. It is considered as early form of leprosy which consists of a skin lesion with slightly less sensitivity to touch. It may resolve or progress further to one of the five forms of leprosy within the Ridley Jopling system. In present study 34 cases (18.5%) were diagnosed as indeterminate leprosy clinically and 16 cases were confirmed histologically. The incidence rate of indeterminate leprosy was very much higher than that than reported by previous studies [12,18,21]. Early detection and diagnosis of indeterminate leprosy is due to increased awareness of the people about leprosy. In indeterminate leprosy, there is mild lymphocytic infiltration around neurovascular bundles, sweat glands and erector pili muscle. No formed epitheloid cell granulomas are observed [22].

Six cases (3.27%) were clinically diagnosed as histoid leprosy; however, on histopathological examination only four cases were diagnosed as histoid leprosy and two cases were turn into LL. Semwal S et al., and Arunagirinathan M et al., were observed complete agreement of clinical and histological diagnosis of histoid leprosy [11,22]. In our study clinico-histopathology concordance was observed in 69.39% of cases. The similar results reported by various other studies [Table/Fig-6] [11,16,18,23-27].

Author [refrence]	Year of study	Place of study	Clinico-histopathology concordence (%)
Mathur MC et al., [23]	2011	Nepal	80.4%
Giridhar M et al., [16]	2012	Amritsar	60.23%
Mohan N and Mishra N, [24]	2013	Uttar Pradesh	56.5%
Kumar A et al., [25]	2014	Rajasthan	62.9%
Rizvi AA et al., [26]	2015	Maharashtra	70%
Banushree CS et al., [18]	2016	Puducherry	79.44%
Semwal S et al., [11]	2018	Bhopal	62%
Ramesh A and Sampath V, [27]	2019	Chennai	61.22%
Present study	2021	Maharashtra	69.39%

[Table/Fig-6]: Clinico-pathological concordance in various studies [11,16,18,23-26].

Maximum clinico-pathological concordence was seen in BT leprosy (82.05%). Similar observations were noted by Mathur MC et al., (80.4%) and Mohan N et al., (56.54%) [23,24].

In 1982, World Health Organisation (WHO) classified leprosy as MB and PB on the basis of BI. Indeterminate leprosy, TT leprosy and BT leprosy cases of leprosy were classified as PB and BB leprosy, BL and LL cases of leprosy were classified as MB [28]. When BI value two or more at any site indicated therapy for MB leprosy and BI value less than two indicated therapy for PB leprosy. The cell mediated immune response and bacterial load is determined by BI. Thus, BI is supportive parameter for the diagnosis and treatment of leprosy patients.

In our study, Fite-faraco stain was positive in all cases of BL leprosy, LL and histoid leprosy. Similar findings were seen in other studies [13,17,18]. Despite specific histopathological findings in different forms, overlapping features are seen in different types of leprosy. Thus, selection of the site for biopsy play an important role in histopathological diagnosis since clinically dissimilar lesions biopsied from the same patient can show different types of histopathology [29]. Hence, it is necessary to correlate clinical, histopathological features along with BI appears to be more useful for accurate typing of leprosy [17].

Limitation(s)

Proper biopsy technique could have contributed to accurate histopathological diagnosis and due to social stigma many patients specially females do not come to hospital because of this actual disease burden remain under reported.

CONCLUSION(S)

There can be significant degree of overlapping clinical features as well as histopathological findings among different types of leprosy. So, concordence of clinical and histopathological features as well as BI should be considered for accurate typing of leprosy. Same is the key to achieve elimination of leprosy cases in the community.

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