Original Article

A study of Clinico-histopathological correlation of leprosy in a tertiary care hospital in western district of Rajasthan

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ABSTRACT

Background: The clinical manifestations of leprosy are so varied and divers and can mimic variety of unrelated diseases, so for the correct and adequate treatment, the diagnosis must be made early and it should be accurate, therefore clinic-pathological correlation is extremely important in patient care.

Aims: To categorize Leprosy into various types based on microscopy and to correlate with clinical presentations.

Materials and Methods: The data base of Department of Pathology, Dr. S. N. Medical College, Jodhpur was reviewed and total 423 clinically diagnosed leprosy patients of all age groups were included in the study.

Results: A total 423 clinically diagnosed leprosy cases evaluated histopathologically. On clinical diagnosis most 74(17.5%) of the cases belonged to Borderline Borderline (BB) leprosy similarly, On histopathological study Borderline borderline (BB) subtype of leprosy was found most 106 (25.06%) common among all subtypes of leprosy and overall Clinico-histopathological agreement was seen in 266 (62.9%) cases and disagreement in 157(37.1%) cases.

Conclusion: The discordance between clinical and histopathological diagnosis was noticed because the clinical diagnosis was made on the basis of Ridley-Jopling classification, even when a histopathological examination had not been made. So instead of using single criterion to diagnose leprosy, the researcher have to consider other contributory factors such as involvement of nerve, skin adnexae, epidermal atrophy, Grenz zone, erosion of the epidermis, granuloma (epithelioid/macrophage) and bacteriological index to arrive at a definitive diagnosis of leprosy.

Key words: Leprosy, clinico-histopathological correlation

INTRODUCTION

Leprosy also known as Hansen's disease and is the oldest disease known to mankind. In India leprosy was first described in susruth samhita written in 600 BC (Lowe 1947) [1]. Leprosy is known, since ancient times as "Kushtaroga", whose clinical manifestations are largely confined to the skin, peripheral nervous system, upper respiratory tract, eyes and testes. The three cardinal sign of the disease are skin lesions, skin anesthesia and enlarged peripheral nerves [2]. Leprosy is one of the leading causes of physical disabilities which contribute to intense social stigma resulting in discrimination of patients and their families.

Although in January 2006 leprosy was eliminated in India but it is still a public health problem in the country [3].

In India a total of 0.92 lac cases were on record as on April 2013, giving a Prevalence rate (PR) of 0.73 per 10,000 population and in Rajasthan 0.12 lac cases were on record as on April 2013, giving a prevalence rate of 0.18 per 10,000 population [4].

The clinical manifestations of leprosy are so varied and divers and can mimic variety of unrelated diseases. Clinical presentation may vary from an insignificant skin lesion to extensive disease causing profound disability/deformities [5].

Leprosy has been classified in a number of ways. The most commonly used is Ridley and Jopling classification (Ridley & Jopling 1962 & 1966) [6]. A new variant of leprosy has been described by Wade in 1960 (Wade 1960). It is known as Histoid leprosy [7].

Histopathological study of leprosy is very important in understanding the disease, its varied manifestation and complications. For the correct and adequate treatment the diagnosis must be made early and it should be accurate. So, clinico-pathological correlation is extremely important in patient care and management.

Fite-Faraco method is used for demonstration of lepra bacilli and it gives information about the infective status and is very helpful in deciding the treatment.

Exact typing of leprosy is sometime clinically not possible and results obtained by slit skin smear are not satisfactory. Therefore histopathological examination is essential in all suspected cases.

This study was undertaken to categorize Leprosy into various types based on microscopy, bacterial index in skin biopsies and to correlate these findings with clinical presentations whenever possible.

MATERIAL AND METHODS

Study area: The present study was conducted at Department of Pathology attached to Dr. S. N. Medical College, Jodhpur, Rajasthan.

Study design and sampling: The data base of Department of Pathology was reviewed and all patients of leprosy were included in the study. Patients with newly diagnosed cases of leprosy were also included. Materials for the study consisted of skin biopsies obtained from patients clinically diagnosed as leprosy who attended the OPD or leprosy clinics of Dermatology Department, Mathura Das Mathur Hospital that is attached to Dr. S. N. Medical College, Jodhpur and histopathology records in Department of Pathology, Dr. S. N. Medical College, Jodhpur.

Study population: A total 423 clinically diagnosed leprosy patients of all age groups were included in the study.

Study period: New cases were included for the period of one and half year (mentioned the duration) and old cases registered in data base of Department of Pathology since January 2008 were included in the study.

Technique: Skin biopsies for the study were obtained by incisional or punch biopsy which was performed by the Dermatologist. These biopsies were kept in 10% formalin and a detailed clinical history, examination findings indicating signs and symptoms of the skin lesions and provisional clinical diagnosis were sent to the Department of Pathology. Following adequate fixation for about 12-24 hours the tissues were submitted into for routine processing, following which the paraffin embedded serial sections of 4-5 microns thickness were obtained, which were stained with Hematoxylin and Eosin for morphological assessment and with modified Fite-Faraco staining for identification of the lepra bacilli.

Data entry and analysis: Data was entered and analyzed by using Micro soft excel version 2007 and Statistical Package for social science ver.16 (SPSS.16) and necessary and appropriate statistical tests were applied and p value less than 0.05 was considered statistical significant.

Ethical clearance: Ethical permission was taken from ethical committee of our institute.

RESULTS

The present study included 423 skin biopsies from 298(70.4%) males and 125(29.6%) female patients who were clinically diagnosed to have leprosy. The age of the patients ranges from 6 years to 90 years with mean of 40.1 years with male to female ratio (M: F) of 2.38 in favour of males.

The majority 101 (23.9%) of the cases belonged to the age group of 21-30 years(3^{rd} decade) and least affected(1.4%) were children below 10 years as shown in table -1.

Ridley-Jopling classification was used to classify leprosy on both clinical and histopathological diagnosis. On clinical diagnosis most of the cases belonged to Borderline Borderline (BB) leprosy {74 cases, 17.5%} and minimum {8 cases, 1.9%} were of Histioid (HL) subtype of leprosy. On histopathology majority 176(41.6%) of cases were in Border line Tuberculoid, Borderline Borderline and Borderline Lepromatous leprosy. On histopathological study Borderline borderline (BB) subtype of leprosy was found dominant 106 (25.06%) among all subtypes of leprosy followed by Tuberculoid (TT) subtype

Table 1: Distribution of histo-pathological diagnosis according to the age

AGE (in yrs)	HISTOLOGICAL DIAGNOSIS								Grand Total
	TT	BT	BB	BL	LL	IL	HL	Unclass-ified	
≤10	0 (0%)	1 (16.67%)	1 (16.67%)	1 (16.67%)	0 (0%)	0 (0%)	0 (0%)	3 (50%)	6 (100%)
11-20	9 (20.93%)	2 (4.65%)	12 (46.5%)	2 (4.65%)	2 (4.65%)	5 (11.63%)	1 (2.32%)	10 (23.25%)	43 (100%)
21-30	25 (24.75%)	8 (7.92%)	28 (27.72%)	9 (8.91%)	6 (5.94%)	6 (5.94%)	4 (3.96%)	15 (14.85%)	101 (100%)
31-40	15 (15.30%)	10 (10.20%)	22 (22.44%)	8 (8.16%)	17 (17.35%)	11 (11.22%)	4 (4.08%)	11 (11.22%)	98 (100%)
41-50	10 (17.24%)	3 (5.17%)	19 (32.75%)	4 (6.89%)	7 (12.07%)	2 (3.45%)	1 (1.72%)	12 (20.69%)	58 (100%)
51-60	12 (18.18%)	6 (9.09%)	15 (22.72%)	4 (6.06%)	6 (9.09%)	6 (9.09%)	4 (6.06%)	13 (19.69%)	66 (100%)
>60	9 (17.64%)	10 (19.60%)	9 (17.64%)	2 (3.92%)	4 (7.84%)	4 (7.84%)	1 (1.96%)	12 (23.52%)	51 (100%)
Grand Total	80 (18.91%)	40 (9.45%)	106 (25.06%)	30 (7.09%)	42 (9.92%)	34 (8.04%)	15 (3.55%)	76 (17.96%)	423 (100%)

(Chi square-42.88, df=42, P value=0.000) TT= Tuberculoid, BT= Borderline Tuberculoid, BB= Borderline borderline, BL= Borderline Lepromatous, LL= Lepromatous, IL= Indeterminate Leprosy, HL= Histoid

Table 2: Clinico-histopathological correlation of leprosy

CLINICAL DIAGNOSIS	HISTOPATHOLOGICAL DIAGNOSIS								Agreement
	TT	BT	BB	BL	LL	IL	HL	Unclassified	
TT (66)	54	5	7	-	-	-	-	-	54(81.82%)
BT (58)	11	20	20	4	2	1	-	-	20(34.48%)
BB (74)	9	8	40	8	9	-	-	-	40(54.05%)
BL (61)	5	5	32	13	4	2	-	-	13(21.31%)
LL (42)	1	1	5	5	27	2	1	-	27(64.28%)
IL (31)	-	-	2	-	-	29	-	-	29(93.56%)
HL (8)	-	1	-	-	-	-	7	-	7(87.50%)
Unclassified (83)	-	-	-	-	-	-	7	76	76(91.56%)
Grand Total	80	40	106	30	42	34	15	76	423

TT= Tuberculoid, BT= Borderline Tuberculoid, BB= Borderline borderline, BL= Borderline Lepromatous, LL= Lepromatous, IL= Indeterminate Leprosy, HL= Histoid Leprosy, Unclassified=UC

Table 3: Different subtypes of leprosy with Kappa statistics

Subtype of leprosy	Kappa	Strength of agreement
TT	0.68	Substantial
BT	0.33	Fair
BB	0.30	Fair
BL	0.21	Fair
LL	0.61	Substantial
IL	0.88	Almost Perfect
HL	0.69	Substantial
UC	0.95	Almost Perfect

Table 4: Comparative study of Clinico-pathological correlation by different authors

Sub-type of leprosy	Sharma A et al[15] (2008)	Pandya A N et al[21] (2008)	Mathur MC et al[18] (2011)	Kansagara et al[22] (2012)	Shivaswamy K N et al[19] (2012)	Giridhar M et al[20] (2012)	Bijjaragi S et al[14] (2012)	Chauhari B et al[17] (2012)	Manandhar U et al[13] (2013)	Thapa D et al[11] (2013)	Singh A et al[12] (2013)	Present study
TT	47.4%	74.5%	73.2%	100%	56%	78.6%	75%	86.2%	24%	66.6%	100%	81.8%
BT	53%	64.7%	89.7%	59.1%	64.1%	73.8%	57.3%	50%	63.2%	42.9%	83.3%	34.5%
BB	37.4%	53.8%	64.7%		50%	-	16.7%	28.6%	0%	-	75%	54.1%
BL	58.8%	28.5%	72.4%	62.5%	73.3%	87.5%	40%	63.3%	57.1%	0%	94.7%	21.3%
LL	75.9%	61.5%	95.2%	54.6%	84.2%	93.8%	76.9%	83.3%	57.1%	16.7%	70%	64.3%
IL	100%	88.8%	-	100%	50%	27.8%	66.7%	-	0%	0%	75%	93.6%
HL	-	-	-	-	-	-	-	-	0%	-	71.4%	87.5%
Overall	53.4%	68.3%	80.4%	66%	74.7%	60.2%	57.3%	70.8%	45.3%		81.7%	
Unclassified	-	-	-	-	-	-	-	-	-	69%	-	91.6%

80(18.9%) and distribution of patients between age and histopathological subtypes of leprosy was found statistically significant (Table 1). All subtypes of leprosy were dominant in males than females.

Overall Clinico-histopathological agreement was seen in 266 (62.9%) cases and disagreement in 157(37.1%) cases (Table 2). Highest (93.5%) clinico-histopathological agreement was found in Intermediate Leprosy (IL) and highest (78.7%) disagreement was found in Borderline Line leprosy (BL). Out of the 83 clinically unclassified cases, 76 (91.56%) were of unclassified and 7 (8.43%) were of Histioid Leprosy (HL) on histopathological study.

Simple agreement, the proportion of agreements between yes and no is a poor measure of agreement because it does not correct for chance. Kappa is the preferred statistic because it accounts for chance and widely used to measure variability between clinical and histopathological diagnosis, that is, how often 2 or more diagnostic methods agree in their interpretations.

Strength of agreement was higher in Tuberculoid (TT), Lepromatous (LL), Intermediate (IL) and Histioid (HL) subtypes of leprosy but was found lower in borderline group as shown in table-3

DISCUSSION

In the present study unclassified and histioid types of leprosy were also included for analysis. In our study majority (47%) of the cases were in 21- 40 years age group (3rd and 4th decade) and least (1.42%) number of cases belonged to cases less than 10 years age group (1st decade). Similarly study conducted by Shegal et al[8], Kaur I et al[9] and Veena S et al[10] also found majority of the cases in 21- 40 years age group (3rd and 4th decade) 52.3%, 48%, and 47.5% respectively and least number of cases in less than 10 years age group (1st decade) 0.96%, 0.2% and 2% respectively.

In the present study majority (70.44%) of the cases were males than females (29.56%) with a sex ratio of 2.38 in favour of males. The results of other studies conducted by Thapa et al[11] (2013), Singh et al[12] (2013) and Manandhar et al[13] (2013) are in congruence with the results of our study having sex ratio of more than 1 in favour of males.
In the present study most (25.10%) of the cases showed predominance of BB subtype, followed by TT (18.90%) cases and BL as a least common (7.10%) type of leprosy. In contrary to our findings study conducted by Bijjaragi et al [14], Manandhar et al [13] and Thapa et al[11] found BT as a most common subtype of leprosy. But in our study most (41.6%) of the cases belonged to borderline group similar to study by Sharma et al[15] and Bijjaragi et al[14] having borderline group 54.8% and 64.9% respectively.

Similar to our study, Veena S et al[10] and Murthy NB et al[16] also found majority of cases of paucibacillary type of leprosy, 77.0% and 85.7% respectively.

The Ridley-Jopling classification is based on clinical, histopathological and immunological features, which is widely accepted by histopathologists and leprologists. The disparity between clinical and histological observations was anticipated because the parameters used for the histopathologic classification are well-defined, precise and also take into account the immunologic response of the tissue, while the clinical classification gives recognition only to the gross appearances of the lesions which is due to the underlying pathological change [17]. So histopathological examination of skin lesions is an important tool in accurate diagnosis and classification of leprosy and still remains the gold standard.

In present study overall clinicohistopathological correlation was found in 266 (62.90%) cases, in congruence to our results majority of the studies also had higher overall correlation (Table-4).

In our study highest (93.6%) correlation was found in IL subtype of leprosy but in contrary to our result, study by Mathur MC et al[18], Shivaswamy KN et al[19], Bijjaragi S et al[14], Giridhar M et al[20] and Manandhar U et al[13] had highest clinico-histopathologic correlation in LL subtype of leprosy, 95.2 %,84.2%,93.8%,76.2% and 57.1% respectively.

In the current study 66 cases was clinically diagnosed as TT, out of which 54 (81.82%) histopathology was confirmed. Of the remaining 12 cases, 5 (7.57%) cases confirmed as BT and 7 (10.61%) cases as BB on histopathology. Similar observations were made by majority of the Authors.

CONCLUSION

The Ridley-Jopling classification is based on clinical, histopathological, bacteriological and immunological features and the discordance between clinical and histopathological diagnosis was noticed because the clinical diagnosis was made on the basis of Ridley-Jopling classification, even when a histopathological examination had not been made. So instead of using single criterion to diagnose leprosy, the researcher have to consider other contributory factors such as involvement of nerve, skin adnexae, epidermal atrophy, Grenz zone, erosion of the epidermis, granuloma (epithelioid/macrophage) and bacteriological index to arrive at a definitive diagnosis of leprosy. In depth studies are required to reassess the criteria, giving weight to different clinical signs and histopathological parameters, in relation to diagnosis of the different types of leprosy.

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