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Research article

CLINICO PATHOLOGICAL CORRELATION OF LEPROSY: A 4 YEARS RETROSPECTIVE STUDY FROM A TERTIARY REFERRAL CENTRE IN NORTH INDIA

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ABSTRACT

Introduction: Leprosy is a chronic infectious disease caused by Mycobacterium leprae that primarily affects the skin and nerves. The histopathological findings in leprosy are related to the immunological status of the patient. **Aim:** To tabulate the incidence of different clinical and pathological patterns of leprosy and establish their correlation. **Materials and Methods:** A total of 118 consecutive skin biopsies of leprosy patients were studied in the Department of Pathology over 4 year duration (2010 – 2014). A Ridley-Jopling criterion was used for the diagnosis and classification of the disease. All biopsies were stained with H&E and Fite Faraco. Clinico-histopathological correlation was calculated using percentage values. **Results:** A total of 118 cases of leprosy were studied out of which 76 were males. The age of the patients ranged from 8 years to 76 years. Majority were in the 31-40 year age group (n= 52.44%). Both clinically (n=55, 46.6%) and histologically (n=41, 34.7%), the maximum patients were in the BT category. Histopathologically LL (21.2%) and BB (16.1%) were the other common groups. The overall concordance between clinical and histopathological classification was 61.8%. Maximum concordance was seen in LL (79.2%) & TT (72.7%). The concordance was lower in borderline groups and least in BL (18.7%). Fite Faraco stain demonstrated acid fast bacilli in 28 cases (23.7%). **Conclusion:** The clinicohistopathological correlation is best at the polar ends of spectrum as compared to borderline cases. Histopathology remains the most powerful indicator of shift in patient's immune status.

Keywords: Leprosy, Clinico histopathological correlation

INTRODUCTION

Leprosy is an infectious disease which was considered a curse to mankind since times immemorial. The earliest possible account for leprosy has been found in ancient Egyptian Papyrus documents as early as 600 B.C. It was Hansen's discovery of causative organism: Mycobacterium leprae in1873 which proved that leprosy was a bacterial disease and not a curse or sin. It occurs more commonly among those living in poverty or overcrowded areas and is transmitted by respiratory droplets. Entry into susceptible host is by respiratory route or broken skin. The disease has a slow incubation period ranging from few weeks to as long as 30 years (average being 3-5 years). India alone reports over 50% of world's leprosy cases.[1]

Skin lesions (macules, papules, nodules), sensory loss and thickened nerves are the reliable signs of leprosy. Positive skin smear for Acid Fast lepra bacilli are considered diagnostic. The WHO system subclassifies leprosy as 'paucibacillary' or

'multibacillary' based on the number of bacteria present. These two types are clinically distinguished by the number of hypopigmented, numb skin patches with paucibacillary having five or less such lesions while multibacillary having more than five[2]. The ICD-10 however uses Ridley-Jopling classification and also adds an indeterminate or 'I' category . Access to information, diagnosis and treatment with Multidrug therapy (MDT) remain the cardinal points in eliminating the disease.

Since 1995 WHO provides free (MDT) to all patients[3]. Prior to starting MDT for particular type of leprosy, the clinical findings should be correlated and confirmed with histopathological examination and bacteriological index of skin biopsy

Aims: To tabulate the incidence of different clinical and histopathological forms of leprosy and to establish their correlation.

MATERIALS AND METHODS

Type of study: Retrospective study

Study place & Duration: Carried out in the Department of Pathology during a 4 year period (2010-2014).

Inclusion Criteria: Cases where histopathological diagnosis of leprosy was made or considered in the differential diagnosis irrespective of age and sex of the patient or nature of the lesion were selected for the study.

Exclusion criteria: Those cases where leprosy was suspected clinically but not confirmed on biopsy were not included. Lepra reactions were excluded.

Ethical Clearance: The present study was approved by the Institutional Ethics Committee.

Methodology: The requisition form accompanying the biopsy specimen as well as the copy of issued histopathology report that were preserved in the Department of Pathology were routinely used to obtain data pertaining to age, sex, clinical information and histopathology findings. The Ridley Jopling criteria was used to diagnose and classify leprosy clinically and histopathologically into the following subgroups: [4]

Tuberculoid (TT): shows epithelioid granulomas with Langhans giant cells surrounded by dense lymphocytic infiltrate. Nerve infiltration is usually seen. AFB is negative.

Borderline Tuberculoid (BT): Epithelioid granulomas with peripheral lymphocytes and Langhans giant cells. Clear subepidermal zone, nerve infiltration present. AFB may or may not be seen.

Borderline(BB): Epithelioid granulomas with diffusely spread lymphocytes, presence of subepidermal clear zone. AFB usually seen.

Borderline Leprosy (BL): Loose granulomas composed of histiocytic cells with dense lymphocytic infiltrate. AFB usually seen but large globi are not present.

Lepromatous Leprosy (LL): Histiocytes and foam cells are abundant. Lymphocytes are scanty, if present they are diffusely spread. Nerves are without cellular infiltrate or cuffing. Grenz zone is present. AFB are numerous.

Indeterminate (I): Lymphocytes and histiocytes are localized around skin structures. AFB are very scanty.

Histoid Leprosy (HLL): Nodular form of leprosy. Microscopy shows circumscribed histoid lepromas characterized by predominance of histiocytes. AFB is numerous.

All the biopsies were fixed in 10% formalin. Serial sections of 5µ thickness were cut and stained with Haematoxylin and Eosin (H&E) along with Fite Faraco to demonstrate Acid Fast Bacilli. Histopathology findings described in detail epidermal atrophy, subepidermal clear zone, distribution and nature of epithelioid granulomas, density of lymphocytes and nerve involvement along with presence of acid fast bacilli.

RESULTS

A total of 118 cases of leprosy were studied over a duration of 4 years (July 2010- July2014). There were 76 males and 42 females. The age of the patients ranged from 8 years to 72 years. Majority of cases (n=52, 44%) were in the 31-40 year age group followed by 23.7 % in the 21-30 year age bracket.

The most common presenting complain was hypo-pigmented patch with loss of sensations (n=67, 56.7%) followed by erythematous macules (n=27,22.8%), nodules (n=14,11.8%) and thickened nerves (n=11,9.3%). (Figures 1,2). All the skin biopsies were taken from the edge of the lesion. Nerve biopsy was not performed in any case.

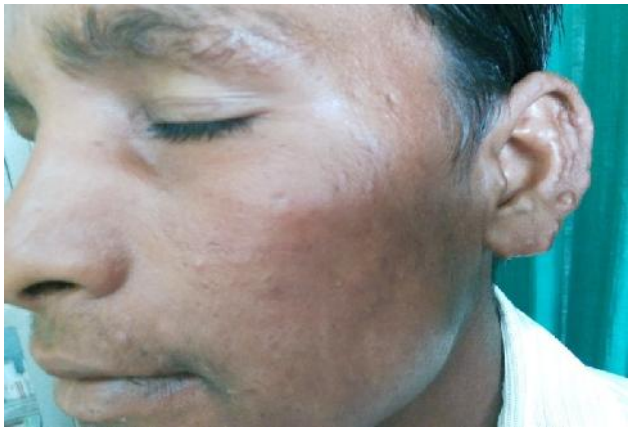

Fig.1 : Lepromatous leprosy

Fig 2: Histoid leprosy

Both clinically (n=55, 46.6%) and histologically (n=41,34.7%), the maximum patients were in the BT category. Histopathologically LL (21.2%) and BB (16.1%) were the other common groups. (Table 1) (Fig 3,4).

Table 1: Clinical and histopathological spectrum of leprosy using Ridley-Jopling classification (n=118)

Clinical Type	No.	%	HPE type	No.	%
TT	11	9.3	TT	17	14.4
BT	55	46.6	BT	41	34.7
BB	06	5.1	BB	19	16.1
BL	16	13.5	BL	07	5.9
LL	24	20.3	LL	25	21.2
IL	01	0.8	IL	05	4.2
Histoid	05	4.2	Histoid	04	3.4
Total	118	100	Total	118	100

The overall concordance between clinical and histopathological classification was 61.8%. Maximum concordance was seen in LL (79.2%) & TT (72.7%). The concordance was lower in borderline groups and least in BL (18.7%). Concordance was 80% for histoid leprosy. (Table 2) (Fig 5). Epidermal changes varied from atrophic (64.8%) to unremarkable to acanthotic. Lymphocytes were most numerous in BB and most scanty in LL. Fite Faraco stain demonstrated Acid Fast Bacilli (AFB) in 28 cases (23.7%). The AFB were mostly seen in LL and HLL forms and only 2 cases in BT type while none in TT type showed AFB positivity. (Fig 6).

Table 2: Correlation of clinical and histopathological diagnosis in leprosy cases (n=118)

Clinical Type	Clinically diagnosed	TT	BT	BB	BL	LL	IL	Histoid	Concordance (%)
TT	11	8	2	-	-	-	1	-	72.7
BT	55	3	36	9	2	1	4	-	65.4
BB	06	-	2	3	1	-	-	-	50.0
BL	16	6	-	3	3	4	-	-	18.7
LL	24	-	1	3	1	19	-	-	79.2
IL	01	-	-	1	-	-	-	-	0
Histoid	05	-	-	-	-	01	-	4	80.0

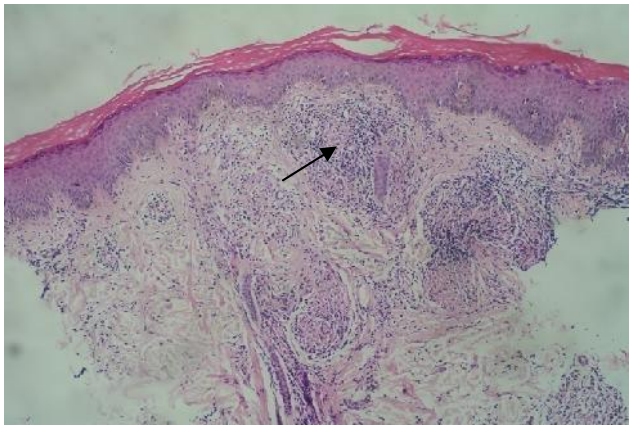

Fig 3: Numerous epithelioid granulomas in BT Hansens (10x10X:H&E:)

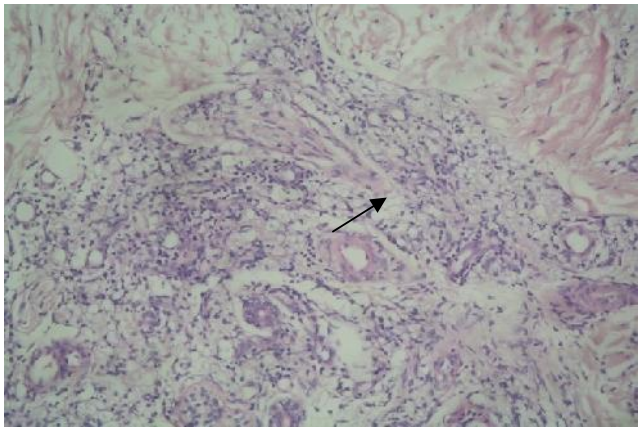

Fig 4: Foamy macrophages in LL Hansens(20x10X H&E)

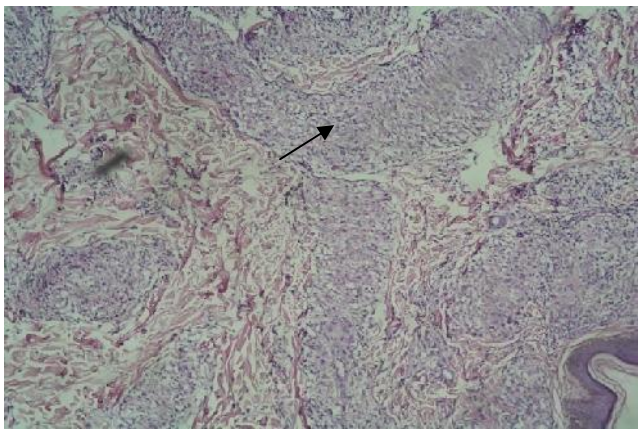

Fig 5: Histoid Hansens disease(20x10X H&E)

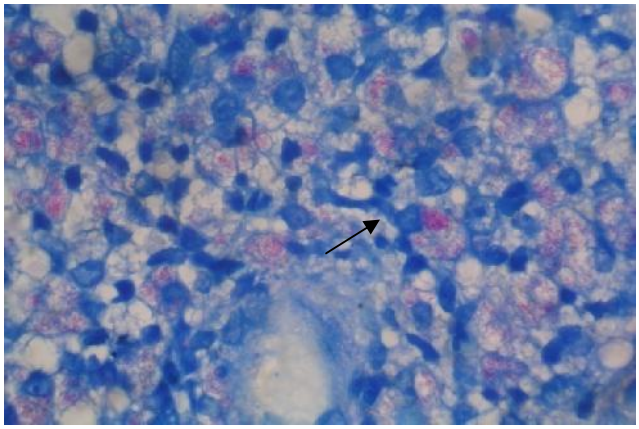

Fig 6: Fite Faraco: Acid Fast Bacilli seen in LL Hansens(100x10X)

DISCUSSION

Leprosy is a chronic infectious disease caused by Mycobacterium leprae and is present in a wide variety of clinical and histopathological forms depending on the immune status of the host. The clinicopathologic correlation studies have provided further insights into the disease, it's manifestations and complications[5]. Ridley-Jopling classification is based upon clinical, histopathological and immunological features and is widely accepted by pathologists and dermatologists. The clinico-pathological discordance is noted because clinical diagnosis is based on Ridley-Jopling classification even when biopsy has not been done[5]. Since biopsy findings may be influenced by biopsy site, age of the lesion, morphology of the lesion, immunological and treatment status of the patient; these may also contribute to discordance between clinical and pathological findings. The best correlation in our study was found with histoid (80%), LL (79.2%) and TT (72.7%). This is similar to study by Bhatia et al, Kalla et al, Kar et al, Jerath et al [6,7,8,9]. Nandkarni et al found 98% correlation in LL form[10]. Correlation is supposed to be better at stable poles LL and TT probably because of clinical and histological stability of the disease. Maximum discordance was seen in midborderline cases as was also noted by Singhi et al, Sharma et al, Manandhar et al, Mitra et al, Moorthy et al [11,12,13,14,15] (Table 3).

Table 3: Comparative study of Clinico-pathological correlation of Hansens disease by different authors

Study	No. of cases studied	% correlation
Present study (2014)	118	61.8
ManandharU et al (2013)[13]	75	45.33
Vargas- Ocampo et al (2004)[16]	6000	42.9
Mitra K et al(2001)[14]	92	57.16
Moorthy BN et al(2001) [15]	372	62.6
Kalla G et al (2000)[7]	736	64.7
Nandkarni NSet al(1999)[10]	2640	81.8
Kar PK et al (1994)[8]	120	70
Bhatia AS et al (1993)[6]	1272	69
Jerath VP et al (1982)[9]	130	68.5
Sehgal VN et al (1977)[18]	95	33

In the present study 5 cases (4.2 %) were diagnosed as Indeterminate leprosy as compared to only 1 case clinically. Indeterminate lesions cannot be classified within Ridley-Jopling spectrum due to lack of distinguishing features like not finding granulomas and this happens more often histologically. All 5 cases in our study diagnosed as IL were clinically TT or BT types. A large study of 6000 cases in Mexico by Vargas-Ocampo encountered LL as the most common form of leprosy[16]. They also found cases of diffuse lepromatosis (Lucio phenomenon) which was not seen in any study done in India. The predominance of LL cases as well as diffuse lepromatosis indicate that a high percentage of population in Mexico has a very low degree of resistance to lepra bacilli as compared to those in Indian subcontinent. In a study by Bal et al , out of 303 leprosy cases , 206 were BT and only 27 were TT. Out of 206 BT cases only 6 were positive for lepra bacilli while none of TT were positive[17]. This was similar to our study where none of TT cases showed AFB positivity. Most previous authors have recorded a higher frequency rate in children (<14 years) and that LL is infrequently seen in this age group[18,19].In our study only 4.2% cases were seen in children and all the cases were of TT+BT subtype.

Though definite diagnosis can be made on histopathological examination, size of specimen, site of biopsy, nature and depth of biopsy, quality of sections, immune status, treatment history and inter-observer variation (both clinically and histologically) should be kept in mind which may lead to clinicopathological discordance[20]

CONCLUSION

Histopathology is the confirmatory test for early diagnosis and proper labelling of all cases of leprosy. It also gives indication of progression or regression of disease under treatment. Clinicopathological correlation of the disease is maximum in polar groups because they are stable and showed a uniform pathology. Maximum disparity is seen in borderline cases because they may have different histopathology in different sites and in different lesions.

Conflict of interest: Nil

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