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Original Article

Clinicohistopathological concordance in Leprosy - A Clinical, Histopathological and Bacteriological study of 100 cases

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Leprosy is a treatable chronic infectious disease, prevalent in South Asian countries, especially India. Before labeling a patient as a case of leprosy and starting multidrug treatment for particular type, the clinical findings should be correlated and confirmed with histopathological examination and bacteriological index of skin biopsy. Skin biopsy is an important tool in diagnosing leprosy and determining the type of leprosy. In the present study, one hundred untreated clinically diagnosed cases of leprosy were studied according to Ridley-Jopling scale for confirmation of diagnosis and classification of leprosy. The study was done by routine H & E (Haematoxylin & Eosin) staining and Fite-Faraco's staining for acid-fast bacillus. The data pertaining to age, sex, clinical and histopathological classification of the type of leprosy were collected and analyzed. In analyzing the histopathology of a lesion, special attention was given to the following features, viz., invasion of the epidermis with or without erosion, involvement of the sub-epidermal zone, character and extent of granuloma, density of lymphocytic infiltrate epithelioid cells and other cellular elements, nerve involvement and the presence of *Mycobacterium leprae.* Histological diagnosis of leprosy was established in 98% of clinically diagnosed cases. Clinicohistopathological concordance was maximum in LL (93.75%) followed by BL(87.5%), TT(78.5%), BT(73.8%) and least in IL(27.78%). Overall, it was 60.23%. Indeterminate type of leprosy was diagnosed more on histology than on clinical evaluation.

Key words : *Mycobacterium leprae,* leprosy, Epithelioid granuloma, Ridley-Jopling criterion.

Introduction

Leprosy is one of the major public health problems of the developing countries. Leprosy, or Hansen's disease, is a chronic infectious disease, caused by *Mycobacterium leprae*.

Leprosy is primarily a granulomatous disease of the peripheral nerves and skin lesions are the primary external symptoms. Leprosy can be progressive and can cause permanent damage to the skin, nerves, limbs, and eyes (WHO 2007). Leprosy is a disease bedevilled by classifications e.g. Madrid classification (ILC 1953), Ridley and Jopling classification (Ridley and Jopling 1966), and Indian classification (IAL 1982). These classifications are based on clinical, bacteriological, immunological and histological status of patients. The standard research classification follows that of Ridley and Jopling, which is based on immuno-

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pathologic data. The histopatho-logical criteria, granuloma cell type, bacterial load (BI), the number and distribution of lymphocytes, pathologic changes in nerves and the presence or absence of the subepidermal grenz zone and encroachment of epidermis form the microscopic basis for the Ridley-Jopling classification.

Leprosy exhibits a spectrum of clinical characteristics that correlate with the histopathological changes and the immunological status of the individual. At one end of the spectrum is Tuberculoid Tuberculoid leprosy (TT), which is manifested with few lesions and a paucity of organisms. At the other end is Lepromatous Lepromatous leprosy (LL), in which there are numerous lesions with myriad bacilli and an associated absence of cellular immune response. In between these poles are Borderline-Tuberculoid (BT), Borderline Borderline (BB) and Borderline-Lepromatous (BL) leprosy. Polar forms (TT and LL) are the most stable and the Borderline forms (BB) the most labile. This categorization is often modified by the addition of subpolar forms at either end of spectrum (TTs and LLs), giving additional categories of subpolar lepromatous leprosy and subpolar tuberculoid leprosy (Ridley 1974). The present study highlights the importance of histopathological examination for exact subtyping of leprosy, so as to facilitate the institution of accurate mode of therapy and regular follow-up of patients to prevent undesirable complications.

Materials and Method

A prospective study was conducted on 100 cases of skin biopsies received as clinically diagnosed cases of Leprosy in the Department of Pathology, Government Medical College, Amritsar from June 2006 to December 2008. New untreated leprosy cases were selected regardless of their age, sex, socioeconomic status and occupation. History of patients was recorded. Clinical examination included the type, number and site of lesions, type of the disease and neural involvement. Skin smears were not done as skin biopsies are more reliable for AFB (acid fast bacillus) positivity. Biopsies were fixed in 10% formalin and processed. Serial sections of 5µ thickness were cut and stained with routine Haematoxylin and Eosin (Culling et al 1985) and Fite Faraco stains (Prophet et al 1994). The Ridley and Jopling classification was followed in both clinical and histopathological diagnosis. In analyzing the histopathology of a lesion, special attention was given to the following features, viz., invasion of the epidermis with or without erosion, involvement of the sub-epidermal zone, character and extent of granuloma, density of lymphocytic infiltrate, epithelioid cells and other cellular elements, nerve involvement and the presence of *M. leprae* (Ridley 1974).

Indeterminate leprosy: Histologically, Indeterminate leprosy is characterized by superficial and deep dermal infiltrate around blood vessels, dermal appendages and nerves, composed predominantly of lymphocytes with few macrophages. No formed epithelioid cell granulomas are present. The diagnosis hinges on finding of one or more acid fast bacilli in the sites of predilection: in nerve, in arector pili muscle, just under the epidermis, or in a macrophage about a vessel. Bacilli are usually difficult to find but following serial sections a single bacillus or a small group of bacilli can be discovered. (Tze-chun et al 1982).

Results

The present study was conducted on 100 cases of skin biopsies diagnosed clinically as leprosy. Out of these, 98% cases were confirmed as leprosy histologically and rest 2% cases were diagnosed as Vitiligo and Lupus Vulgaris. These 2% cases were excluded from further study. There were 76(77.6%) male cases as compared to 22 (22.4%)

female cases. Maximum numbers of cases were in the age group of 21-30 years i.e. 41 (41.8%) cases. Cases from rural area i.e. 66.6% were higher than cases from urban area i.e. 34 (34.6%). Maximum numbers of cases were laborers i.e. 34(34.6%) followed by service employee i.e. 29(29.6%).

Leprosy more commonly presented with hypopigmented patch with 68 (69.4%) cases than as erythematous plaques with 30 (30.6%) cases. As shown in table 1, amongst patients presenting with hypopigmented patch, 82.35 %(TT-25% and BT-57.35%) patients were towards tuberculoid pole of leprosy and 78.13% patients were towards lepromatous (LL-50% and BL-28.13%) pole amongst patients with erythematous plaques.

Most common site chosen for biopsy was upper limb in 39.80% cases (arm 16.33%, forearm 17.35%, hand 5.10% and finger 1.02%) followed by 28.57% cases from back and 22.45% from lower limb.

Clinically, BT was the most common type of leprosy with 44% cases followed by TT 18% cases, LL 17%, BL 14%, IL 5% and least common type of leprosy seen clinically was BB with 2% cases. (Table 2) On histopathological examination of received biopsy stained with H & E, diagnosis were TT 14.25%, BT 42.86%, BL 8.16%, LL 16.33% and IL 18.37% cases.

Out of 98 sections, of histologically proven cases of leprosy, stained with Fite Faraco stain,

Table 1 : Showing clinical presentation in various types of leprosy

Clinical diagnosis	Hypopigmented patch		Erythematous plaque /papule/ nodule	
	No. of cases	%age	No. of cases	%age
TT	17	25.00	01	03.13
BT	39	57.35	05	15.63
BB	01	01.47	01	03.13
BL	05	07.35	09	28.13
LL	01	01.47	16	50.00
IL	05	07.35	-	-
Total	68	100.0	30	100.0

Table 2 : Showing clinical and histopathological distribution of leprosy cases

Type of leprosy	Clinical		Histopathological	
	No. of cases	%age	No. of cases	%age
TT	18	18.0	14	14.25
BT	44	44.0	42	42.86
BB	2	2.0	0	0.0
BL	14	14.0	8	8.16
LL	17	17.0	16	16.33
IL	5	5.0	18	18.37
Total	100	100.0	98	100.0

55(56.13%) cases showed presence of acid fast bacilli in histological sections and 43(43.87%) cases lacked acid fast bacilli. No acid fast bacillus could be demonstrated in any of the case of TT. (Table 3) Amongst cases of BT, 13 out of 42(30.95%) cases showed presence of acid-fast bacilli with 8(18.6%) cases with BI of 1+ and 5(11.6%) cases with BI of 2+. Rest 29(69.05%) showed absence of acid-fast bacilli. No case of BB was diagnosed in present study. All histologically diagnosed cases of BL i.e. 8(100%) cases and BL, 16(100%) cases showed presence of acid fast bacilli. Amongst BL cases, 2(25%) cases showed BI of 3+, 5(62.5%) and 1(12.5%) cases showed BI of

Table 3 : Showing positivity of AFB in different types of leprosy

Type of leprosy	Positive		Negative		Total
	No. of cases	%age	No. of cases	%age	No. of cases
TT	-	0	14	100.0	14
BT	13	30.95	29	69.05	42
BB	-	-	-	-	-
BL	08	100.0	0	0.0	08
LL	16	100.0	0	0.0	16
IL	18	11.11	0	88.89	18
Total	55	56.13	43	43.87	98

Table 4 : Showing Bacterological index in various types of leprosy

	Bacteriological index						
	0	1+	2+	3+	4+	5+	6+
TT	14(100%)	-	-	-	-	-	-
BT	29(69.0%)	8(18.6%)	5(11.6%)	-	-	-	-
BL	-	-	-	2(25%)	5(62.5%)	1(12.5%)	-
LL	-	-	-	-	-	4(25%)	12(75%)
IL	-	18(100%)	-	-	-	-	-

Table 5 : Correlation between clinical and histopathological classification

Histopathological diagnosis	Clinical diagnosis						% age of agreement
	TT	BT	BB	BL	LL	IL	
TT (14)	11	03	-	-	-	-	78.57
BT (42)	03	31	01	06	01	-	73.81
BB (0)	-	-	-	-	-	-	-
BL (8)	-	-	-	07	01	-	87.50
LL (16)	-	-	-	01	15	-	93.75
IL (18)	03	09	01	-	-	05	27.78
Total (98)	17	43	02	14	17	05	

Table 6 : Concordance of type diagnosis of leprosy by two modes of examination expressed as percentage for each mode of examination

Classification	Concordance of diagnosis	
	Correlated cases / Histologically diagnosed cases%	Correlated cases / Clinically diagnosed cases %
TT	78.57	64.71
BT	73.81	72.09
BB	-	-
BL	87.50	50.0
LL	93.75	88.24
IL	27.78	100.0

Table 7 : Showing percentage of overall parity observed in different studies

	Year of study	Overall parity (%)
Mitra and Biswas	2000	57.6%
Kumar et al	2000	60.6%
Singh et al	2000	58.6%
Pandya and Tailor	2008	58%
Present study	2009	60.23%

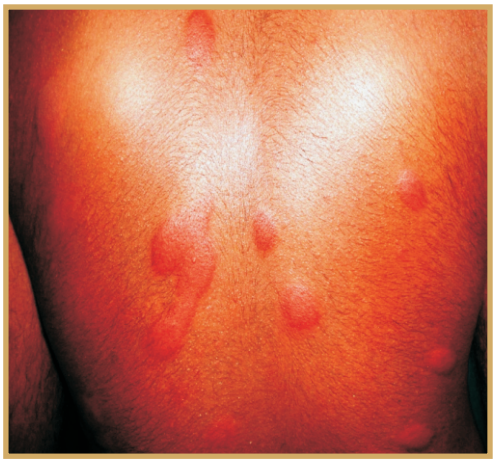

Fig 1 : Borderline Lepromatous Leprosy showing numerous erythematous maculopapules

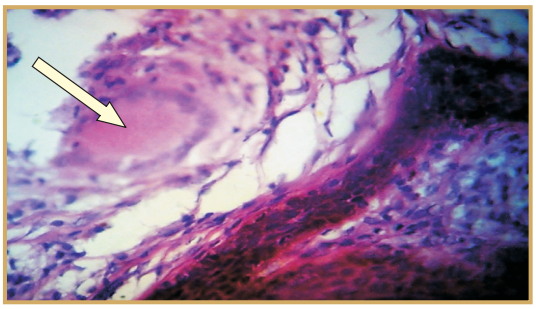

Fig 2 : Tuberculoid leprosy showing Langhans type giant cell (arrow) (H&E400x)

4+ and 5+ respectively. Amongst LL cases 4(25%) cases were with BI of 5+ and 12(75%) cases with BI of 6+. 18(100%) cases of IL showed BI of 1+. (Table 4)

On correlating clinical and histopathological diagnosis (Table 5), maximum percentage of agreement of 93.75% was shown in LL type of leprosy with 15 cases diagnosed both clinically as well as histopathologically. This was followed by Borderline Lepromatous leprosy with percentage of agreement between clinically and histo-

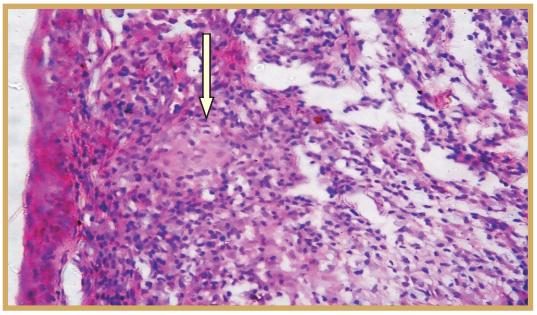

Fig 3 : Borderline Tuberculoid Leprosy showing ill defined granuloma (arrow) (H&E400x)

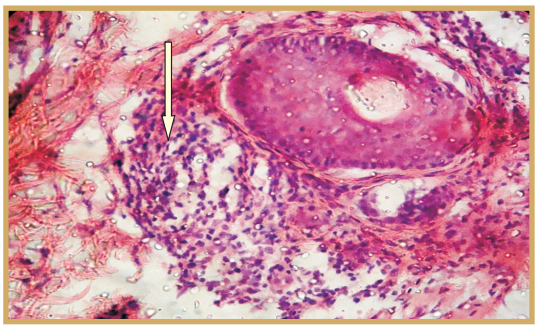

Fig 4 : Showing periappendageal infiltration in indeterminate leprosy (arrow) (H &E 400x)

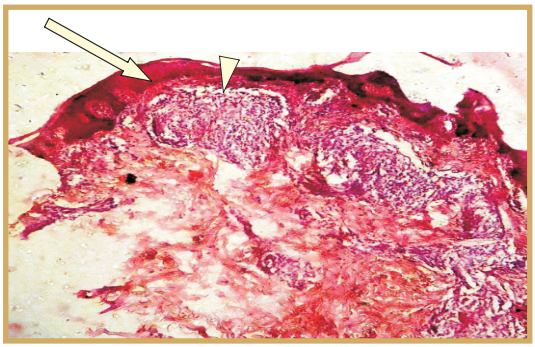

Fig 5 : Lepromatous Leprosy showing Grenz zone (arrow) and macrophage granuloma (arrow head) (H&E 100x)

pathologically diagnosed cases being 87.5%, followed by TT (78.57%), then by BT (73.81%). Least agreement was seen in cases of indeterminate types of leprosy i.e. 27.78%, cases were diagnosed more on histopathology as compared on clinical evaluation. Overall agreement was 60.23%.

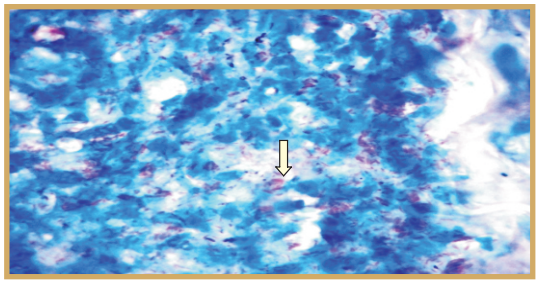

Fig 6 : Lepromatous Leprosy with BI 6+ showing acid fast bacilli (arrow) (Fite stain 400X)

Table 6 shows that histopathological concordance was seen maximum for LL (93.75%) type than for other types and was least for indeterminate type of leprosy (27.78%) whereas clinical concordance was maximum for indeterminate type of leprosy (100%).

Discussion

Leprosy is widely prevalent in India. There were 0.83 lakh leprosy cases as on April Ist 2011 with prevalence rate of 0.69 per 10,000 population (NLEP 2011). Leprosy is a chronic, infectious disease caused by *Mycobacterium leprae* and is present in different clinico-pathological forms, depending on the immune status of the host. The study of pathological changes in leprosy lesions has contributed a great deal to understanding the disease and clinico-pathological correlative studies have provided further insights into the disease, its varied manifestations and complications (Kalla et al 2000).

Out of 100 cases studied 77.6% patients were males and 22.4% females with a male-to-female ratio (M:F) of 3.46:1. Almost similar results were

obtained in study conducted by Bhushan et al in 2008 and there were 72.34% males and 27.66% females. The male:female ratio was 2.61: 1.

In present study, hypopigmented patches/ macules were the lesions most frequently biopsied (68%) and in these skin lesions, features of TT, BT, IL were frequently found and out of 32% cases of erythematous nodules/plaques/papules, most of cases showed features of BL and LL. Similar results were obtained in a study by Vargas-Ocampo and Francisco(2004), in which macules were the lesions most frequently biopsied, and in these skin lesions the features of TT, BT, and IL were more frequently found. The nodule was the most significant lesion for LL. In a study by Mittal et al in 1996, 63/102 (61.76%) cases had hypopigmented macules and 38.24% cases had erythematous nodules. Midborderline leprosy is immunologically the least stable and present with variety of clinical lesions of different morphology, so this type of leprosy is difficult to diagnose.

In the present study 74.52%, cases were of paucibacillary and 24.48% of multibacillary type of leprosy. This study was in contrast to retrospective study done by Tiwari et al from 1994 to 2009 on 3659 cases and they found 80.57% MB cases and 19.43% PB cases (Tiwari et al 2011). This difference can be attributed to regional variation and different socioeconomic and immune status in population studied.

In the present study histological diagnosis of leprosy was established in 98% cases. One case (1%) was diagnosed as case of Vitiligo and another (1%) as Lupus Vulgaris. Similarly in a study by Singh et al in 2000, histological diagnosis of leprosy was established in 104 cases (93.69%) out of 111 cases. In study Bhatia et al (1993) on 1272 cases, 1204 (95%) cases were histologically diagnosed as leprosy and 68(5%) were reported as "no evidence of leprosy" by the histo-pathologists. In study by Ocampo and Francisco, 96.85% cases were histologically confirmed to be of leprosy and rest 3.15% cases with the clinical diagnosis of leprosy showed histological findings of dermatosis different from leprosy. Of these, the majority were interpreted as being neuro-fibromatosis, atopic dermatitis, and pityriasis alba. In contrast, in study by Cortes and Rodriguez (2004), leprosy was confirmed by histopathology in 119 cases (57.5 percent) out of 207 biopsies and in study by McDougall et al (1987), only 52% (354) of the biopsies out of 684 showed definite evidence of leprosy on histopathological examination. The discrepancy is due to clinical overdiagnosis of leprosy and misinterpretation of many skin conditions presenting with hypo-pigmented patch as leprosy. Selection of the site for biopsy plays an important role in the histopathological diagnosis since clinically dissimilar lesions biopsied from the same patient can show different types of histopathology.

In the present study, complete parity between clinical type and histopathological type was noted in 60.23% cases. A comparison of parity is tabulated in Table 7.

In the present study, Parity for individual type of leprosy was found to be TT (78.57%), BT (73.81%), BB (0%), BL (87.5%), LL (93.75%) and IL (27.78%). In study by Pandya and Tailor in 2008, parity for individual type of leprosy was TT (66.7%) BT(53.3%), BB(0), BL(36.3%), LL(83.3%) and IL(87.5%). In a study by Moorthy et al (2011), while correlating the histopathological diagnosis with clinical diagnosis, maximum correlation (80%) was noted in LL patients followed by BL(70%), BT(66.54%), BB(50%), TT (46.15%) and it

was very poor in IL (20%). Mitra et al (2000) in a study of 736 patients observed highest parity in LL and TT group (76.7% and 75.6%), respectively, followed by BT (44.2%), BL (43.7%) and BB (37.0%).

Considering the data of present study and other comparative studies, parity in the polar group was maximum, and was seen in Lepromatous lepromatous leprosy which because of their stability showed a fixed histopathology. Few clinically diagnosed cases of TT and BT (3 cases of TT and 9 cases of BT shown in Table 5), were categorized as cases of Indeterminate leprosy because of non specific histopathological features.

Conclusion

We conclude from our study that histopathological examination along with bacteriological index of skin biopsy should be carried out in all cases of leprosy to arrive at a definite diagnosis of leprosy and to classify the type of the disease.

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