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To Study the Spectrum of Leprosy in a Regional Tertiary Referral Centre of Uttarakhand

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Abstract
Background: *Leprosy (Hansen's disease) - a communicable disease still continues to be a social stigma and leading cause of permanent physical disability. This can be prevented by early histopathological diagnosis and adequate treatment accordingly.*
Objectives: *The aim of the present study was to evaluate the spectrum of different clinico-histopathological categories of leprosy.*
Material and Methods: *This study was conducted from September 2016 - August 2018, in the Department of Pathology & Skin and Venereal disease on 62 untreated, clinically suspected cases of leprosy.*
Statistical Analysis: *Descriptive analysis was done in the form of percentage or proportions. P value < 0.05 was considered significant.*
Results: *In this study 62 cases of leprosy diagnosed as per Ridley-Joplings (R-J) clinical classification were evaluated histopathologically. Most of the cases were seen in young adult males. Majority of cases (42 cases; 67.74%) presented with erythematous lesions and 20 cases (32.25%) presented with hypopigmented lesions. Multiple skin lesions and multiple nerve involvements were commonly seen in lepromatous spectrum. Lepromatous leprosy (LL) was the most common type of leprosy (24 cases; 38.70%) clinically. Indeterminate leprosy (IL) (21 cases; 33.87%) was most common type on histopathological examination. The clinico-histopathological correlation was highest in IL and tuberculoid leprosy cases. Overall correlation was seen in 36 cases (58.06%).*
Conclusion: *As clinical diagnoses of early leprosy lesions are difficult due to lack of cardinal signs hence biopsy should be done in all cases in order to improve classification and treatment.*
Keywords: *Clinical, histopathological, leprosy, lesions, spectrum.*

Introduction

Leprosy originates from the Latin word 'Leprosus' meaning defilement. India represents approximately 60% of global burden of leprosy. [1] WHO defined three key objectives in April 2016, under the motto "2016-2020 accelerating towards a leprosy- free world." Mycobacterium leprae (M.leprae) has predilection for Schwann cells

(SCs) and cause injury to the peripheral nerves with demyelination and consequent disability Depending on immune status of the host leprosy expresses itself in different clinico-pathological forms.[2],[3] On the basis of clinical, bacteriological, histopathological and immunological features, Ridley-Jopling classified leprosy into tuberculoid (TT) leprosy at the one end of spectrum which manifests with few lesions, and at the other end is lepromatous leprosy (LL) which present with numerous lesions containing myriads of bacilli and absence of cellular immune response [4]. The present study aimed to categorize leprosy into various types clinically and histomorphologically.

Material and Methods

Spectrum of 62 untreated and clinically suspected cases of leprosy was studied in the Department of Pathology & Skin and V.D in a government medical college of Uttarakhand from September 2016 - August 2018.

Detailed history and thorough clinical examination was done, including general, systemic and cutaneous examination particularly with reference to skin, nerves, sensory and motor disturbances in the following sequence:

Palpation of the commonly involved peripheral and cutaneous nerve was done such as ulnar nerve near the median epicondyle, greater auricular nerve as it turn over sternocleidomastoid muscles, lateral popliteal and the dorsal branch of the radial nerve for the presence of thickening and / or tenderness.

Testing for loss of sensation for heat, cold, pain and light touch in the skin patches was done.

Examination for paresis or paralysis of the muscles of the hand and feet was done for detection of disabilities or deformities.

Lesions of leprosy were classified according to the R-J clinical classification and then biopsies with 4-6mm size punch needle were taken from the most active and untempered lesions. Biopsies were stained with Haematoxylin & Eosin **(**H&E), Wade- Fite stain to demonstrate lepra bacilli and the histopathological categorization was done according to the R-J criteria.

Statistical Analysis: It was done in term of chi-square test. Percentage or proportions were used for descriptive analysis. P value < 0.05 was considered significant. Microsoft Excel 2010 data analysis tool and SPSS (Statistical Programme for Social Science) version 16.0 for windows were used for data analysis.

Result

The present study included 62 patients who were clinically suspected to have leprosy. Patients of age group of 11-20 years were most commonly affected (16 cases; 25.80%) followed by 13 cases (20.96%) in age group of 31-40 years and lowest number of cases were from age group of 1-10 years i.e. 2 cases (3.22%). There were 38 (61.29%) male patients and 24 (38.70%) female patients (M: F= 1.58:1). Majority of cases (42 cases; 67.74%) presented with erythematous lesions [Figure-1] and 20 cases (32.25%) presented with hypopigmented lesions [Figure-2], [Figure-3]. Among the hypopigmented lesions, macules were the most common lesion (17 cases; 85%) and among the erythematous lesions, combinations of different types of lesions (20 cases; 47.61%) were most commonly seen [Table-1]. Greater than 5 lesions were more likely to occur in lepromatous spectrum of cases, [Figure-4] while fewer lesions [Figure-5] were more likely to occur in the tuberculoid spectrum [Table-2].

Multiple sites were involved in 38 cases (61.29%) followed by lower extremity involvement in 12 cases (19.35%). In IL, lower extremity was the most commonly involved site while in Tuberculoid (TT), LL, Borderline lepromatous (BL) and Borderline borderline (BB) leprosy, multiple site involvements were most commonly seen [Table-3].

Majority of cases (32 cases; 51.61%) presented with hypoesthesia and 9 cases (14.51%) presented with anaesthesia. In varied histological subtypes of leprosy cases, the percentage of number of

cases with skin sensation loss are increased but in BL cases there is decrease in percentage of cases with loss of skin sensation from 72.72% to 27.27% and this difference is significant statistically (P value: 0.041).The proportion of leprosy cases of different histological types having complete loss of skin sensation is fewer [Table-4].

Ulnar nerve was the most commonly involved nerve in 16 cases (25.80%) followed by combined involvement of radial and ulnar nerve in 7 cases (11.29%). Multiple peripheral nerve thickenings were more towards the lepromatous pole, while one or no nerve involvement was more towards the tuberculoid pole [Table-5].

Out of total 62 cases, other associated findings such as trophic ulcers, clawing of hands, madarosis, nasal deformities were seen in 15 cases (24.19%) of which nasal deformity and epistaxis (5 cases; 8.06%) were the most common finding, followed by oedema of hands and feets (4 cases; 6.45%). Clawing of hand (1 case; 1.61%) was the rare finding.

On clinical diagnosis most of the cases belonged to LL (24 cases; 38.70%) followed by borderline tuberculoid (BT) (19 cases; 30.64%) and minimum cases belonged to TT (2 cases; 3.22%) subtype of leprosy [Table-6]. On histopathology majority of cases were in IL group (21 cases; 33.87%), followed by LL (16 cases; 25.80%) and minimum cases belonged to borderline borderline (BB) (1case; 1.61%) [Table-7]. The Clinico-histopathological agreement was highest in IL (7 cases; 100%) and TT (2 cases; 100%) cases followed by BL (6 cases; 60%) and was least in Borderline tuberculoid (BT) (7 cases; 36.84%) leprosy. On doing agreement analysis (Kappa test) between the clinical and histological classification of different subtypes of leprosy cases, there was fair agreement in making diagnosis of inderminate (IL), borderline tuberculoid (BT) and BL as the kappa value was <0.5, while in making diagnosis of TT and LL the kappa value was slightly >0.5. Overall clinico-histopathological correlation was seen in 36 cases (58.06%) [Table -8]. On examination of histological sections after Wade-Fite staining it was observed that no acid fast bacilli could be demonstrated in any of the case of indeterminate leprosy. Amongst 5 cases of TT only one case showed the presence of bacilli while amongst the 16 cases of LL all showed presence of acid fast bacilli.

Table 1: Types of skin lesions

Types of lesion	Macule	Papule	Nodule	Combination of lesions
Erythematous	3(7.14%)	1(2.38%)	6(14.28%)	20(47.61%)
Hypopigmented	17(85%)	0(0%)	0(0%)	0(0%)

Table 2: Association between number of skin lesions and histopathological diagnosis

Histopathological group	Total no. of cases	=1	2-5	>5
IL	21	7(33.33%)	10(47.61%)	4(19.04%)
TT	5	0(0%)	2(40%)	3(60%)
BT	8	0(0%)	6(75%)	2(25%)
BL	11	0(0%)	2(18.18%)	9(81.81%)
LL	16	0(0%)	0(0%)	16(100%)
BB	1	0(0%)	0(0%)	1(100%)

Table 3: Distribution of site involvement according to histological groups

Site	Histological types of leprosy					
	IL(21)	TT(5)	BT(8)	BL(11)	LL(16)	BB(1)
Upper extremity	5(23.80%)	0(0%)	1(12.50%)	1(9.09%)	0(0%)	0(0%)
Lower extremity	9(42.85%)	0(0%)	1(12.50%)	1(9.09%)	1(6.25%)	0(0%)
Head and neck	1(4.76%)	0(0%)	3(37.50%)	0(0%)	1(6.25%)	0(0%)
Multiple sites	6(28.57%)	5(100%)	3(37.50%)	9(81.81%)	14(87.50%)	1(100%)

Table 4: Association of loss of skin sensation and different histological subtypes of leprosy

Sensation	IL (21)	TT (5)	BT (8)	BL (11)	LL (16)	BB (1)	P value
Normal	6 (28.57%)	0 (0%)	3 (37.50%)	8 (72.72%)	4 (25%)	0 (0%)	Chi sq likelihood ratio value is 18.929 Df=10 P value is 0.041
Hypoesthesia	13(61.90%)	2 (40%)	4 (50%)	3 (27.27%)	9 (56.25%)	1 (100%)	
Anaesthesia	2 (9.52%)	3 (60%)	1 (12.50%)	0 (0%)	3 (18.75%)	0 (0%)	

Table 5: Association of number of peripheral nerve involvement and histopathological diagnosis

Histopathological group	Total no. of cases	No nerve involved	Single nerve involved	>1 nerve involved
IL	21	18(85.71%)	3(14.28%)	0(0%)
TT	5	3(60%)	1(20%)	1(20%)
BT	8	3(37.50%)	4(50%)	1(12.50%)
BL	11	4(36.36%)	1(9.09%)	6(54.54%)
LL	16	6(37.50%)	0(0%)	10(62.50%)
BB	1	0(0%)	1(100%)	0(0%)
Total	62	34(54.83%)	10(16.12%)	18(29.03%)

Table 6: Clinical spectrum of various types of leprosy

Clinical diagnosis	No of cases	Percentage(n=62)
IL	7	11.29%
TT	2	3.22%
BT	19	30.64%
BL	10	16.12%
LL	24	38.70%
Total	62	100%

Table 7: Histopathological diagnosis of leprosy

Histological Type	No. of cases	Percentage (n=62)
IL	21	33.87%
TT	5	8.06%
BT	8	12.90%
BL	11	17.74%
LL	16	25.80%
BB	1	1.61%
Total	62	100%

Table 8: Clinico-histopathological assessment agreement of leprosy:

Histopathological groups									
Clinical groups		IL	TT	BT	BL	LL	BB	Agreement	Disagreement
	IL (7)	7	0	0	0	0	0	7(100%)	0(0.00%)
	TT (2)	0	2	0	0	0	0	2(100%)	0(0.00%)
	BT (19)	8	1	7	1	2	0	7(36.84%)	12(63.15%)
	BL (10)	2	1	0	6	0	1	6(60%)	4(40.00%)
	LL (24)	4	1	1	4	14	0	14(58.33%)	10(41.66%)
	Total(62)	21	5	8	11	16	1	36(58.06%)	26(41.93%)

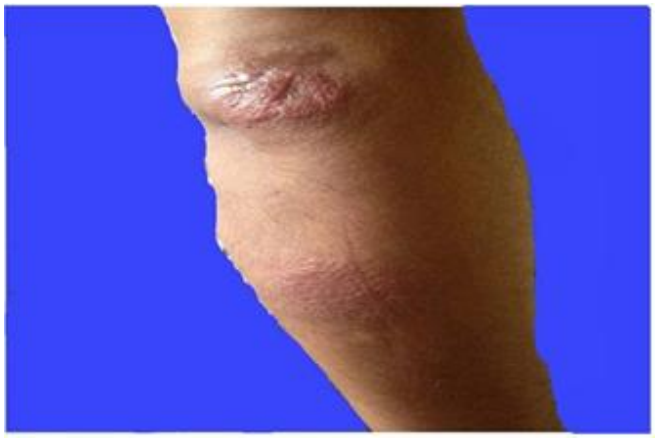

Figure 1: Borderline lepromatous leprosy showing copper coloured multiple shiny infiltrated plaques on elbow and forerm.

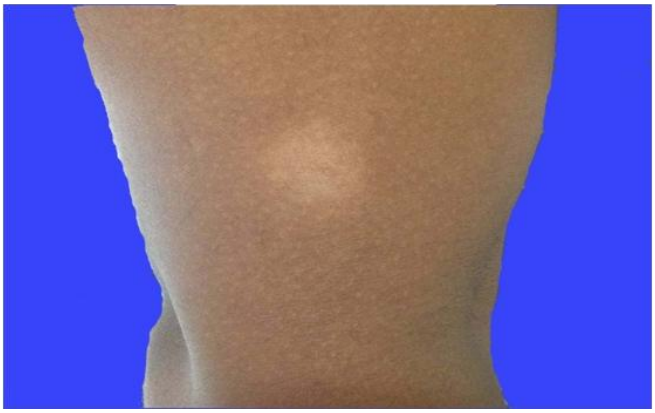

Figure 2: Indeterminate leprosy: revealing hypopigmented poorly demarcated macule over forearm.

Figure 3: Tuberculoid leprosy: A large well defined raised hypopigmented lesion (Plaque).

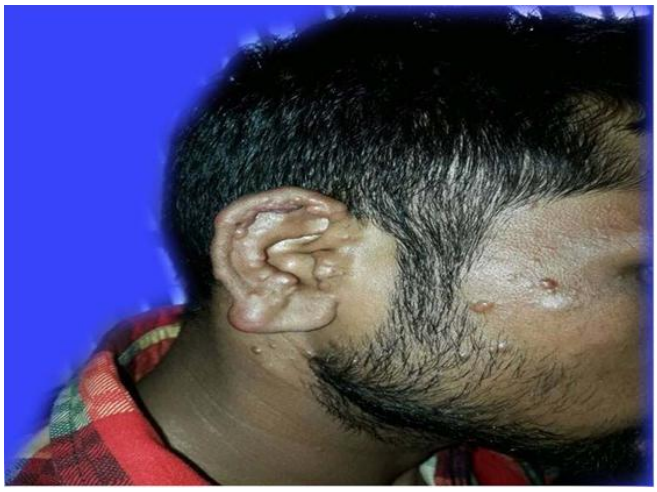

Figure 4: Lepromatous leprosy with multiple lesions and infiltrations of earlobes.

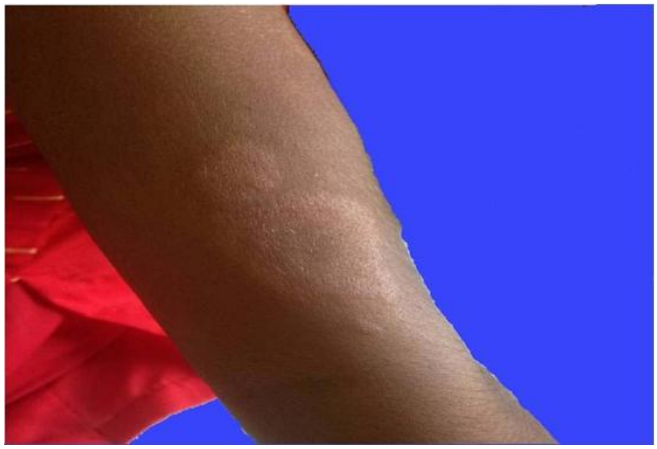

Figure 5: Borderline tuberculoid leprosy: well demarcated lesion with small satellite lesions.

Discussion

Leprosy, a chronic granulomatous infection present commonly with skin lesions. In this study age group of 11-20 yrs (16 cases; 25.80%) was most commonly affected, but in contrary to our results study done by Valand et al[5] and Kumar A et al [6] found maximum number of cases in the age group of 21-30 yrs. Children of age group of 1-10 yrs were affected least (2 cases; 3.22%), this can be explained by the variable and long incubation period. Male predominance (M: F: 1.58:1) in our study has also been reported in many previous studies.[7][8] Illiteracy, poor knowledge and under reporting of leprosy in females may be the factors responsible for the male predominance. Among the hypopigmented lesions, macules (17 cases;

85%) were the most common lesions similar to observations made by Tiwari M et al[9] and Badhan R et al.[10] In contrast to this, study done by Shresta et al[11] and Kumar SA et al[12] showed plaques as the most common presenting lesions. In our study majority of cases in lepromatous spectrum presented with greater than 5 skin lesions, while cases in tuberculoid spectrum presented with fewer skin lesions, similar to observations made by AC Lobo et al [13] and Tiwari M et al [9]. Our study showed majority of patients (41 cases; 66.12%) presented with hypoesthesia / anaesthesia, similar to observation made by Bommakanti J et al [14] and Kumar SA et al. [12] Multiple site involvement was most commonly seen (38 cases; 61.29%) followed by lower limb involvement (12 cases; 19.35%), while study done by Shresta A et al [11] showed upper limb as the most common site of skin lesions.

In our study multiple peripheral nerve involvement was commonly seen towards the lepromatous pole while one or no nerve involvement was most commonly seen towards the tuberculoid pole, similar to observation made by AC Lobo et al.[13] Ulnar nerve was the most commonly involved nerve in 16 cases (25.80%) followed by combined involvement of radial and ulnar nerve in 7 cases (11.29%), similar to observation made by Shresta et al.[11] The bacterium complex cell wall contain large amount of M. leprae specific phenolic glycolipids (PGL-1) and this unique tri-saccharide binds to the basal lamina of Schwann cells of axons.

In our study, trophic ulcer were seen only in 2 cases (13.33%), similar to observation made by Kumar SA et al[12] in which trophic ulcer was seen in 1 case (1.70%). Deformities such as claw hand was seen in 1 case (6.66%), similar to observation made by Bommakanti J et al [14] in which claw hand was seen in 3 cases (6.8%).

According to Ridley Jopling's classification, maximum number of cases (24 cases; 38.70%) clinically belonged to the lepromatous leprosy group, while the study conducted by Nadia S et al[7] showed majority of patients in borderline tuberculoid group. The increased number of lepromatous leprosy in our study can be attributed to the different socioeconomic and immune status of population studied. This can be resolved by better education, increased awareness and stringent implication of national leprosy eradication programmes.

Histopathologically, IL (21 cases; 33.90%) constituted the major group, followed by LL (16 cases; 25.80%), similar to observations made by Arunagirinathan M et al. [15] In contrast to our study, BT was the most common type in the study done by other authors. [10], [16] Highest percentage of IL noted histopathologically in our study could have been due to immunological differences in host responses. This can be resolved by appropriate selection of site (s) and adequate depth of the biopsy to be taken.

In our study highest agreement in clinico-histopathological diagnosis was seen in IL and TT cases similar to observation made by Kansagra et al [17], while the study done by other authors showed highest clinico- pathological correlation in LL cases. This may be due to different selection criteria used in different studies as Mathur NK et al[18] has selected only case with macular lesions in their study, while in our study all types of skin lesions has been included such as macules, plaques, nodules etc. Similarly in some studies both treated and untreated patients were selected, whereas in our study only untreated patients were included.

The present study showed an overall agreement in clinico-histopathological diagnosis in 36 cases (58.06%). The disparity between clinical and histopathological diagnosis was noticed in 26 cases (41.93%). It is logical to expect disparity between the clinical and histopathological features as there is variable tissue response due to variability of cell mediated immunity in different individuals and regions which is also evident in our study. Clinical sign and symptoms may precede the known characteristic tissue changes or vice versa in some early cases. If a biopsy is taken at an early stage there is likely to be discordance

between the clinical and histopathological observation.

Conclusion

Although leprosy can be classified clinically by observing number and types of skin lesions and nerve involvement, but there can be some degree of overlap between different types of leprosy cases clinically. So for accurate typing of disease, biopsy and histopathological examination is considered gold standard.

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