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Hansen's disease: Is histopathological correlation mandatory for all clinically diagnosed patients? A descriptive study in a tertiary care hospital

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ABSTRACT

Background: Leprosy has been historically associated with social stigma and discrimination. Leprosy, also known as Hansen's disease, is indeed a chronic infectious disease caused by the bacterium *Mycobacterium leprae*. Diagnosis of leprosy is usually done by clinically and classified as multibacillary (MB) and paucibacillary (PB). The disease was also classified into different types based on histopathological findings, such as tuberculoid, borderline tuberculoid (BT), mid-borderline, borderline lepromatous, and lepromatous. **Aims and Objectives:** The aim of the study was the clinicohistopathological correlation of all clinically diagnosed cases of Hansen's disease. **Materials and Methods:** The study was done at Bankura Sammilani Medical College and Hospital for a period of 18 months. Ethical approval was taken from the Institutional Ethics committee. All new patients 66 in number clinically diagnosed as leprosy attending the Dermatology Outpatient Department were included in the study. The skin biopsy and staining were done with hematoxylin and eosin staining and Fite-Faraco stain for every patient. The skin biopsy was reported according to the Ridley-Jopling classification. **Results:** Males were more commonly affected than females. Most of the leprosy cases in the study were classified as MB (86.4%) and the upper extremities were the most commonly affected sites. Bacterial index was observed negative in clinically PB cases. The most common histological subtype of leprosy identified in the study was BT, Regarding bacterial index, all clinically diagnosed MB cases were smear positive and PB cases were smear negative. Out of nine clinically diagnosed PB cases, inflammatory cells were found in 3 (33.4%). **Conclusion:** In a large country like India where resources are limited, no need for skin biopsy for every patient. Biopsy should do if there is any confusion with other skin lesions.

Key words: Clinicohistopathological correlation; Hansen's disease; Leprosy

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INTRODUCTION

Leprosy, also known as Hansen's disease, is indeed a chronic infectious disease caused by the bacterium *Mycobacterium leprae*. It is believed to be transmitted through respiratory droplets, much like the common cold. However, it is a relatively slow-growing bacterium, and not everyone exposed to it becomes infected. In addition, with early diagnosis and appropriate treatment, the risk of transmission is significantly reduced. It is true that a significant portion of the population is naturally resistant to leprosy. The exact reasons for this resistance are not fully understood, but it is believed to be related to genetic factors. Not everyone exposed to the bacteria will develop the disease. Leprosy primarily affects the skin and peripheral nerves. It can manifest in various forms, from mild and non-contagious (tuberculoid leprosy) to more severe and potentially contagious (lepromatous leprosy). The

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symptoms can range from skin lesions to nerve damage, which can lead to deformities if left untreated. Diagnosis of leprosy is typically based on clinical evaluation, which includes a thorough examination of the skin and nerves. In some cases, a skin biopsy may be performed to confirm the presence of the bacteria. Leprosy has been historically associated with social stigma and discrimination. This stigma is due in part to misconceptions about the disease's contagiousness and fear of disfigurement. However, with increased awareness, education, and effective treatment, the stigma associated with leprosy has been decreasing over the year. Leprosy is treatable with multi-drug therapy, a combination of antibiotics that kill the bacteria. Early diagnosis and timely treatment are essential to prevent the progression of the disease and associated complications, such as physical disabilities. Proper treatment not only cures the disease but also reduces its contagiousness.

Diagnosis of leprosy is usually done by clinically and classified as multibacillary (MB) and paucibacillary (PB). Due to clinical diversity of disease and ability to mimic many other skin lesion, it is very difficult to diagnose clinically in early stages.[1] In this context, the study was done to correlate between histopathological findings and clinical pattern of all clinically diagnosed leprosy cases.

Aims and objectives

The objective of the study was to correlate between histopathological findings and clinical pattern of all clinically diagnosed Leprosy cases.

MATERIALS AND METHODS

The study was conducted at Bankura Sammilani Medical College and Hospital in West Bengal. It was a hospital-based comparative study with cross-sectional. The study period was 18 months from January 2021 to June 2022. Ethical approval was taken from Institutional Ethics committee (no. BMCH/Aca 202 Dated January 01, 2021). All new patients clinically diagnosed with leprosy attending the Dermatology Outpatient Department were taken. According to the prevalence of leprosy, the estimated sample size was 57. All clinically diagnosed new cases that were given consent for biopsy were included in the study. Old cases (already received anti leprosy treatment), relapse cases, and critically ill patients were excluded from the study. Hence, the final participant was 66 in number.

Data collection was conducted with the help of pre-designed semi-structured scheduled containing demography profile. Detailed clinical examinations were done for every patient including number of skin lesions, nerve involvement, and any deformity. A standard criterion for diagnosis and classification (IAL 1982, Ridley and Jopling 1966) and grading of disabilities as per World Health Organization (WHO) criteria (Brandsma and van Brakel 2003) was followed. These cases were classified into PB and MB types as per the WHO criteria.

Slit Skin Smear Chodavadia et al. 2023 examination was done, histopathology findings were noted and analyzed for these leprosy cases. The leprosy patients were essentially classified according to the IAL classification (Mishra and Kataria, 2017) - The clinical types diagnosed included lepromatous leprosy (LL), borderline lepromatous (BL), mid borderline (BB), borderline tuberculoid (BT), tuberculoid (TT), pure neuritic (N), and indeterminate leprosy.

The skin biopsy was done as an out-patient procedure for every patient in dermatology department. Biopsy was taken from the most active lesions. The biopsy material was placed immediately in a container having 10% formalin as fixative. Then, the material sent to the Pathology department. Hematoxylin and eosin staining and Fite-Faraco staining were done in all cases. The skin biopsy was reported according to the Ridley-Jopling classification.[2]

RESULTS AND ANALYSIS

Demographic profile

The mean±standard deviation age of all participants was 39.57±15.04 years with range of 11 to 75 years. The minimum age of patient, this was a female of 11 years and maximum age of patient which was 75 years of male patients. Maximum numbers of clinically diagnosed leprosy occurs in between age group 41–50 years which were 16 (24.2%) and minimum numbers of age group was above 60 years of age which 6 (9.1%) cases were considering both sexes. The age distribution was not related with sex. Number of total female was 23 (34.8%) and male was 43 (65.2%) and male and female ratio was 1.87:1. Among the patients in our study, maximum were by occupation cultivation which were 20 (30.3%) followed by house wife 19 (28.8%).

Clinical disease spectrum

Among all patients of the present study, clinically highest numbers were MB (86.4%) than PB (13.6%). MB cases were more in male (70.2%) than female (29.8%) but in case of PB, female (66.7%) were more than male (33.3%). In our study, it was shown that most of the lesions found in upper extremities (39.4%), followed by face (31.8%), trunk (16.7%), and lower extremities (12.1%). Study showing that ≤1 number of nerve involvement were 14 (21.2%) and >1 number of nerve involvement were (74.2%) and total 3 (4.6%) cases had no nerve involvement. In the study, it was found that in clinically 57 of MB cases, 56 cases had

more than five skin lesions and one case had less than five skin lesions. In PB cases, all the cases had less than five skin lesions. According to the nerve involvement, MB cases had ≤1 were 8 and >1 were 49 and in PB cases had ≤1 were 6 and 0 nerve involvement were 3.

Smear positivity and histopathology

Regarding bacterial index, all clinically diagnosed MB cases were smear positive and PB cases were smear negative. Study showed that bacterial index among the MB cases, 2+ were maximum (45.5%) and 5+ were minimum (6.1%) in between that 1+ was (12.1%), 3+ was (12.1%) and 4+ was (10.6%) (Table 1).

Among the different types of clinically diagnose, MB leprosy cases hiatopathologically BT were maximum 38 (66.7%) followed by BL 17.5% and LL 9 (15.8%). Cases of PB BT were maximum 4 (44.4%) and TT were 2 (22.2%). Out of nine clinically diagnosed PB cases, inflammatory cells were found in 3 (33.4%) (Table 2). Figures 1-4 showing different histopathology and acid fast bacilli in leprosy patient.

Study showed that bacterial index among the cases, 2+ is maximum which was 30 (45.5%) and 5+ is minimum which is 4 (6.1%) in between that 1+ was 8 (12.1%), 3+ was 8 (12.1%) and 4+ was 7 (10.6%). It was shown that 57 (84.8) patients were positive and 9 (15.2%) were negative.

In our study, it was found that in clinically diagnose MB and PB cases histopathologically BT was most where there was no TT case in MB and PB had 2 TT cases. In case of PB there were 4 BT cases followed by 3 inflammatory cells. In case of MB, 10 cases were BL and 9 cases were LL.

Table 1: Distribution of patients according to bacillary index (n=66)

Bacillary index	Frequency	Percentage
One positive	8	12.1
Two positive	30	45.5
Three positive	8	12.1
Four positive	7	10.6
Five positive	4	6.1
Negative	9	13.6
Total	66	100.0

Table 2: Distribution of leprosy cases according to clinical diagnosis and histopathological correlations

Histopathological type	MB (57)		PB (9)	
	No.	Percentage	No.	Percentage
TT	0	0	2	22.2
BT	38	66.7	4	44.4
BL	10	17.5	0	0
LL	9	15.8	0	0
Inflammatory cells	0	0	3	33.4
Total	57	100	9	100

MB: Multibacillary, PB: Paucibacillary, TT: Tuberculoid, BT: Borderline tuberculoid, BL: Borderline lepromatous, LL: Lepromatous leprosy

DISCUSSION

Hansen's disease is a slowly progressive, chronic infectious disease which can express itself in different clinicopathological forms depending on immune status of the host.[3] It primarily affects the skin and the peripheral nerves. It can be progressive and can cause permanent damage to the skin, nerves, limbs, and eyes. The study was undertaken for the clinical and pathological study of newly diagnosed leprosy patient to fulfill the aims and objectives of present study. It was carried out in Bankura Sammilani Medical College. A disease like leprosy needs an appropriate classification because of its varied manifestations. The most commonly accepted classification by research workers is that of Ridley and Jopling. which is primarily based on immunity but has been correlated with clinical, histopathological and bacteriological findings. In the present study, the cases were classified histopathologically into TT, BT, BB, BL, and LL. During the study, we found clinically diagnosed nine pure neuritic cases but due to PN case have not been confirmed by histopathologically so these cases were excluded. During study, we found that in three clinically diagnosed PB cases, histopathologically only inflammatory cells found and these cases are negative for leprosy. In addition to the differential diagnoses of leprosy are, granuloma multiformis, lupus erythematosus, superficial mycoses, pityriasis alba, pityriasis versicolor, dermatophyte, cutaneous leishmaniasis, etc. Hence, it is very important to confirm leprosy cases by histopathologically examination; otherwise, these cases will be diagnosed falsely as the leprosy cases and will be wrongly treated. Leprosy can occur at all age groups. In the present study, majority of the patients were in the age group of 41–50 years (24.2%), followed by 21–30 years (22.7%), 31–40 years (19.7%), 51–60 (13.6%), 11–20 years (10.6%), and ≥61 years (9.1%). The patients mean age of presentation was 39.57±15.04. These findings are comparable with those of Kumar et al.,[4] Bhushan et al.,[5] Mehta et al.,[6] Chhabra et al.[7] The male and female ratio in our study was 1.87:1 which was seen in a study conducted by Nadia's et al.[8] (1.8:1) and Moorthy et al.[9] 66 clinically confirmed cases were studied where male are 43 and female 23. The male preponderance for leprosy noted in our study was also been shown in other studies like Manandhar et al.,[10] Semwal et al.[11] and Vargas-Ocampo. This might be attributed to increased chances of exposure due to increased job-related mobility. In our study, among the 66 new cases, the WHO classification identified 57 (86.4%) cases of MB, as compared to the result of Rawat et al.[12] Another study where MB predominance is also reported

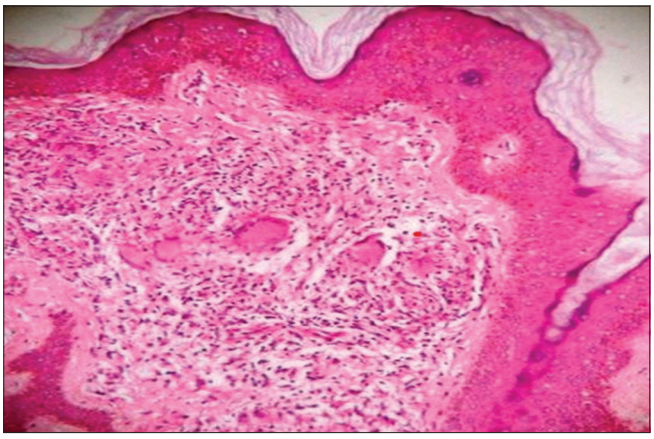

Figure 1: Tuberculoid leprosy (wellformed granuloma with Langhans giant cells and lymphocytic infiltration)

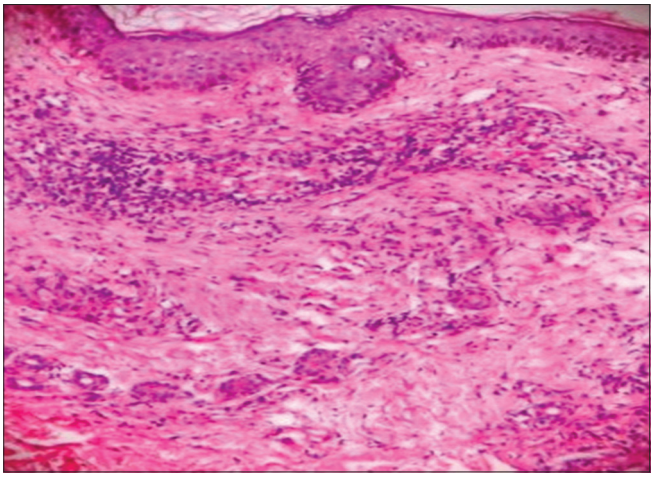

Figure 2: Inflammatory lesion, only lymphocytic infiltration

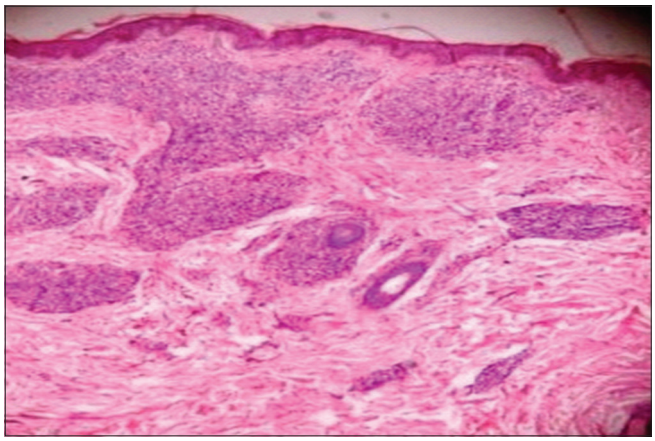

Figure 3: Lepromatous leprosy (atropic epidermis, grenz zone and nodular aggregates of foamy cells and scant lymphocytes)

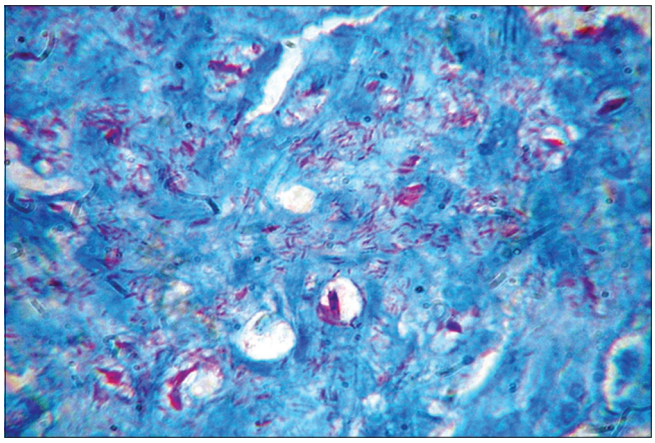

Figure 4: Acid fast bacilli in small clusters. (Modified Fite-Faraco stain)

found by Singal and Sonthalia,[13] Jindal et al.,[14] and Thakkar and Patel.[15] In the study, it was found that MB cases are more in male (70.2%) than female (29.8%) and PB cases are more in female (66.7%) than male (33.3%). MB cases are more in male than female was studied in other studies like Swati et al.[16] Regarding the skin involvement, 56 (84.8%) patients presented with more than five skin lesions and 10 (15.2%) patients presented with <5 skin lesions. The most common primary sites of the lesions in the present study were upper extremities 26 (39.4%), followed by face 21 (31.8%), trunk 11 (16.7%), and lower extremities 8 (12.1%). This result is comparable with the findings of Tekwani et al.[17] and Semwal et al.[11] Tekwani et al.[17] studied the clinico histopathological correlation in different types of leprosy and observed that the upper extremity was the primary site of lesion which was 34.81%, followed by the face 29.62%, trunk 14.81%, the lower extremities 11.85%. Nerve involvement is also a cardinal sign of leprosy and more than 1 nerve involvement was seen in 49 (74.2%), one nerve involvement was seen in 14 (21.2%), and 0 nerve involvement was seen in 3 (4.6%) of cases in our study. In our study it was found that clinically one MB case had less than five skin lesions but it was diagnosed clinically MB as it had more than one nerve involvement and eight MB cases had ≤1 nerve involvement but these cases were diagnosed as clinically MB by more than five skin lesions. Bacterial Index is 0 in all cases of clinically PB (9) among which three were inflammatory cases. And among clinically 57 MB cases, all were bacteriologically positive in modified Acid fast Bacilli (AFB) stain. 11 had 1+, 31 had 2+, six had 3+ again six had 4+, and three had 5+ in bacteriological index. This similar study found in Naik et al.,[18] Tiwari et al.,[19] Giridhar et al.[20] In our study, we found negative bacterial index in all PB cases and among MB case most of the cases (47%) were 2+ bacillary index where study by Naik et al.[18] it was mostly (22%) 1+ bacillary index. The demonstration of AFB is still considered important for diagnosis, classification and treatment of leprosy. In our study, 57 (84.8%) patients were positive and 9 (15.2%) were negative. Sixty-six clinically confirmed new leprosy cases are taken as study sample. The most common histologic subtype recorded in our study was of BT which was 42 (63.6%). BT has been reported to be

the most common histological type of leprosy in other studies like, Moorthy et al.,[9] Tekwani et al.[17] (57.77%) and in the study conducted by Singh et al.[21] and Mehta et al.[6] It was consequently 31.7% and 26%. The second most common histopathological diagnosis in the current study was related to the patient with BL, which was 10 (15.2%). This result in line with the results achieved by Tekwani et al.,[17] Singh et al.[21] LL was detected in 9 cases (13.6%) in the present study. Similar observation was noted in the studies of Singh et al.[21] (13.3%) and Mehta et al.[6] (20%) while 5.8% of the cases and 9.5% of cases were identified in the studies conducted by Tekwani et al.[17] and Kadam et al.,[22] respectively. TT was detected in 2 (3%) cases in present study. The similar type of study was conducted by Naik et al.[18] (8%), Singh et al.[21] (10%) while the most TT cases were found in the studies of Tekwani et al.[17] (19.25%), Kadam et al.[22] (19%) and Mehta et al.[6] (26%).

Majority of study population were agricultural workers 20 (30.3%) followed by housewife 19 (28.8%), small business man 13 (19.7%), students 11 (16.7%), and unemployed 3 (4.5%).

Limitations of the study

Our study has limitations of data from one hospital only which may not be representative of situation in the urban and rural communities of this area. Properly designed epidemiological studies and interventions should be undertaken at community levels.

CONCLUSION

Most of the previous study concluded that biopsy should mandatory for the diagnosis and classification of Leprosy. In our study, all clinically diagnosed MB cases were bacillary positive and PB cases were bacillary negative. Out of nine PB cases, biopsy of three patients showed no granuloma but inflammatory cells. May be these three patients clinically over-diagnosed as Leprosy. In a large country like India where resources are limited no need for skin biopsy for every patient. Biopsy should do if there is any confusion with other skin lesion.

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SK- Definition of intellectual content, Literature survey, Prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation, and submission of article; **ND-** Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **SB-** Design of study, statistical Analysis, and interpretation; **SJ-** Literature survey and preparation of figures; coordination, and manuscript revision, **SD**- data collection and data analysis, **SS-** Concept, design, and clinical protocol.

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