Clinicopathological correlation of Hansen's disease: a retrospective study of skin biopsies

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Abstract

Background: Hansen's disease is a curable chronic infectious disease. The clinical presentation and histopathological interpretation of skin biopsy may show variations as various types of the disease exist. The clinical diagnosis should be confirmed by histopathological features and bacteriological study before starting treatment for particular type of the disease.
Materials and Methods: A retrospective hospital based study was conducted among patients with clinically diagnosed Hansen's disease classified according to Ridley-Jopling scale. Skin biopsy taken from active lesion was stained with routine Haematoxylin & Eosin (H & E) stain and modified Fite-Faraco's stain for acid-fast bacillus
Results: Out of 107 histologically confirmed cases, male to female ratio was 1.6:1. The age of the patients ranged from 4-80years. Clinically, BT was the most common type of leprosy with 43% cases followed by TT 20.64% cases, LL 14.95%, BL 13%, IL 8.41% and least common type of leprosy seen clinically was BB with 0% cases. The commonest type on histopathology was BT with 39.25% followed by TT 19.62%. The correlation was highest in lepromatous leprosy(100%).The Clinical and histopathological correlation was seen in 85 cases (79.44%)
Conclusion: There can be overlap between different types of leprosy, both clinically and morphologically. So correlation of clinical and histopathological features along with bacteriological index appears to be more useful for accurate typing of leprosy. The concordance was high in LL. BB is rarely diagnosed both clinically and histopathologically.

Keywords: Leprosy, Acid-fast bacilli, Granuloma, Foamy macrophage

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Introduction

Hansen's disease (Leprosy), an ancient curable chronic infectious disease, still continues to be a significant health problem in developing countries. Leprosy is caused by *Mycobacterium leprae* bacillus, that affects mainly peripheral nerves and skin but may also affect other sites such as the eyes, mucous membranes, bones, and testes and produces a spectrum of clinical types.[1-3] The presence of bacilli in the skin produces the dermatological manifestations of the disease, and nerve infection produces axonal dysfunction and demyelination, leading to sensory loss and its consequences of disability and deformity.[2,5] The term Leprosy is a tribute to the Norwegian physician Gerhard Armauer Hansen, who identified the bacillus *Mycobacterium leprae* as the cause of the disease in 1873.[6] In 1966, Ridley–Jopling classified leprosy according to clinical, bacteriological, immunological, and histological criteria into TT (Tuberculoid Tuberculoid), BT (Borderline Tuberculoid), BB (Borderline Borderline), BL (Borderline Lepromatous), and LL (Lepromatous Lepromatous).[7] In 1982, WHO proposed simplied classification of pauci and multibacillary leprosy based on clinical findings and the bacteriological index to facilitate diagnosis and treatment of leprosy in the field.[8] However, Ridley-Jopling classification is widely accepted by pathologists and leprologist. Clinical diagnosis in some cases can be difficult which can lead to occurrence of resistant cases if treated inadequately. Skin biopsies play an important role in diagnosing and classifying different types of leprosy.[5]

Materials and Methods

A hospital based retrospective study was conducted in department of Pathology in a tertiary care hospital by collecting the clinical data and histopathological report from medical records section after obtaining ethical committee approval of our Institute.

Punch biopsies taken from clinically diagnosed new skin lesion of leprosy was taken. History regarding age, sex, site, type of the lesion and clinical classification was noted. Skin specimen fixed in 10% formalin, processed and sectioned. Slides were stained by Hematoxylin-Eosin (HE) and modified Fite-Faraco's stain. Ridley-Jopling criteria was used to classify the disease histopathologically and Clinically.[7] On microscopic examination, 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, giant cells, nerve involvement and the presence of acid fast bacilli was noted. Diagnosis of Indeterminate leprosy was made in cases 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.[9] Leprosy cases presenting with clinical manifestations or histopathological changes suggestive of lepra reactions were excluded from the study.

Results

The present study was conducted on 110 cases of skin biopsies diagnosed clinically as leprosy. Out of these, 97.3% cases were confirmed as leprosy histologically and 2.7% cases were excluded from further study. A total of 107 cases of leprosy were included in the present study out of which 63(58.9%) were males and 44(41.1%) were females.

Male to female ratio was 1.6:1. The age of the patients ranged from 4 years to 80 years. Majority of the patients, 44 were in the age group below 30 years(41.1%), followed by 42(39.3%) between 31-50 yrs and 21(19.6%) above 51years (Table 1).

Most of the patients presented with hypopigmented patch in 70 cases (65.4%) followed by erythematous plaque and nodule. Most common site was upper limb 76 cases(71%), followed by back and lower limb. Clinically, BT was the most common type of leprosy with 43% cases followed by TT 20.64% cases, LL 14.95%, BL 13%, IL 8.41% and least common type of leprosy seen clinically was BB with 0% cases. The commonest type on histopathology was BT with 39.25% (Fig. 2) followed by TT 19.62% (Fig. 1). The Clinical and histopathological correlation was seen in 85 cases (79.44%). The correlation was highest in lepromatous leprosy(100%) followed by borderline lepromatous(100%) and borderline tuberculoid(83.33%) (Table 2). Fite Farraco stain was positive in 33 cases (30.84%) (Fig. 4). No acid fast bacillus could be demonstrated in any of the case of TT. All histologically diagnosed cases of BL and LL showed positivity for bacilli. Epidermal erosion and ulceration was more commonly seen in TT and BT(24.3%). Grenz zone and macrophages was noted in all cases of lepromatous leprosy (Fig. 3). Epithelioid granuloma was noted in all cases of TT. Perineural lymphocytic infiltrate was seen in all cases of BL and IH (Fig. 5)(Table 3).

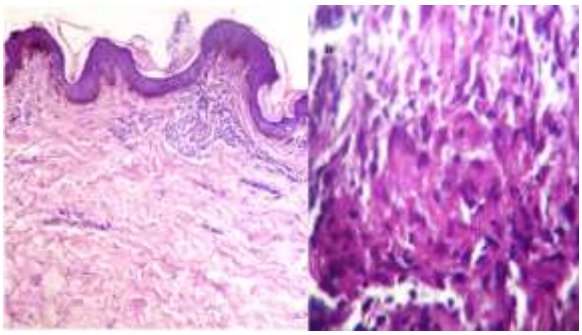

Fig. 1: a. Microphotograph (10X; H&E) showing well formed epithelioid cell granuloma eroding the epidermis.
b. Microphotograph (40X; H&E) showing epithelioid cell granuloma in Tuberculoid leprosy

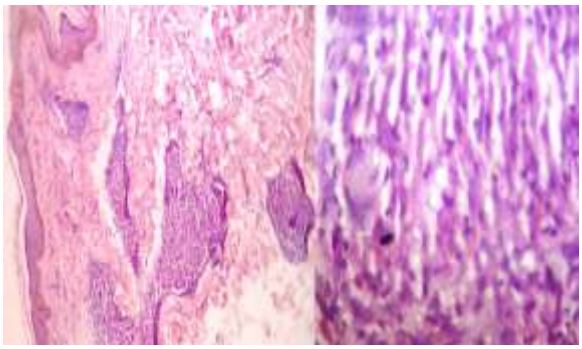

Fig. 2a & b: Microphotograph (10X & 40X; H&E) showing ill-defined granuloma with langhans type of giant cell in boderline tuberculoid leprosy

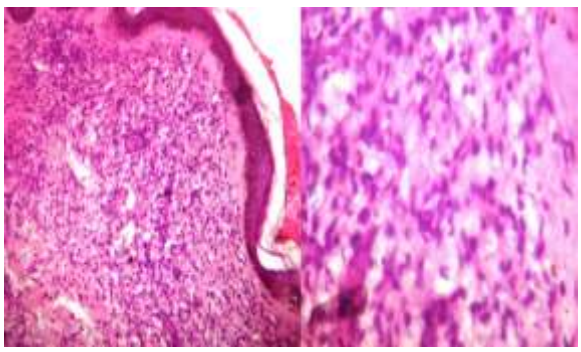

Fig. 3 a & b: Microphotograph (10X & 40X; H&E) showing atrophic epidermis, grenz zone and diffuse macrophage infiltration in lepromatous leprosy

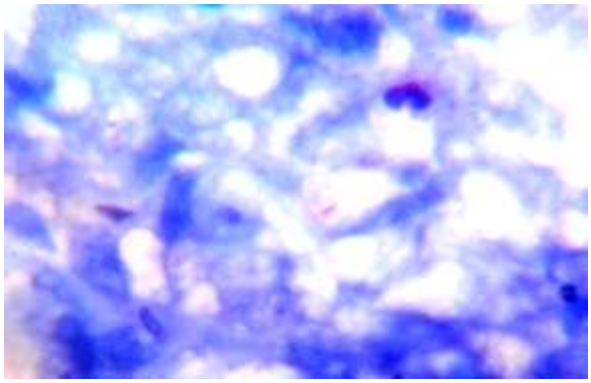

Fig. 4: Fite stain (100X) showing acid fast bacilli in lepromatous leprosy

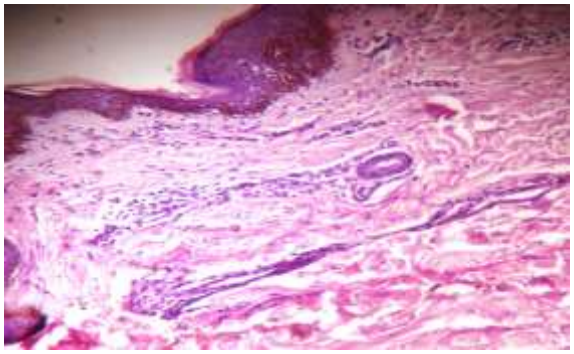

Fig. 5: Microphotograph (10X; H&E) showing periappendageal and perivascular lymphomacrocytic infiltration in indeterminate leprosy

Table 1: Showing age distribution in the subjects

Age group(years)	Number of cases	Percentage (%)
Below 30	44	41.1
31-50	42	39.3
Above 50	21	19.6
Total	107	100

Table 2: Clinico- histopathological Correlation

Histopathological diagnosis	Clinical diagnosis						% of agreement
	TT	BT	BB	BL	LL	IL	
TT(21)	17	3	-	-	-	1	81
BT(42)	2	35	-	5	-	-	83.33
BB(0)	-	-	-	-	-	-	-
BL(10)	-	1	-	9	-	-	90
LL(16)	-	-	-	-	16	-	100
IL(18)	3	7	-	-	-	8	44.44
Total	22	46	0	14	16	9	

Table 3: Histopathological Changes observed in Epidermis and Dermis in Leprosy

Epidermal change							
	TT (21)	BT (42)	BB (0)	BL (10)	LL (16)	IL (18)	Total (107)
Atrophic	1	10	-	5	16	-	32(29.9%)
Erosion/Ulceration	14	11		1			26(24.3%)
Unremarkable	6	21	-	4	-	18	49(45.8%)
Dermal change							

Epithelioid granuloma	21	27	-	-	-	-	48(44.85%)
Giant cell	13	1	-	-	-	-	14(13.08%)
Periappendageal lymphocyte	14	27	-	10	2	11	64(59.81%)
Perineural lymphocyte	2	17	-	10	9	18	56(52.33%)
Macrophages	-	-	-	10	16	3	29(27.10%)
Grenz Zone	-	2		8	16	-	26(24.3%)

Table 4: Showing clinicopathological correlation in various studies

	Year of study	Clinico-pathological correlation
Kumar et al	2000	60.6%
Pandya et al	2008	58%
Mathur et al	2011	80.4%
Giridhar et al	2012	60.23%
Rizvi et al	2015	70%
Present study	2016	79.44%

Discussion

Leprosy can vary clinically among patients, with a clinical spectrum that extends from the polar "tuberculoid" to the polar "lepromatous" form of the disease.[10,11] The tuberculoid form is characterized by a small number of hypopigmented, well-bordered, anesthetic skin lesions with a low bacillary load , early peripheral nerve impairment, and a T-helper 1 (Th1)–mediated immune response. In contrast, the lepromatous form is characterized by numerous infiltrated skin lesions displaying high bacillary loads, impaired peripheral nerves, possible involvement of internal organs, and a Th2-mediated immune response.[12] Most common age group affected in leprosy was 20-30 years and was least common below the age of 10 years may be because of longer incubation period.[13] The number of leprosy cases in adults is reported to be higher among men, with a male to female sex ratio ranging between 1.5 and 2 and in our present study it was 1.6.[14] In TT, histopathologically well-formed epithelioid cell granulomas with a rim of lymphocytes distributed throughout the dermis, particularly along adnexal structures and neurovascular bundles and enroaching the basal layer of the epidermis will be seen. In BT, granulomas have fewer number of lymphocytes and more giant cells and epidermal erosion will not be seen. Erosion into the epidermis with absence of Grenz zone when present is a useful feature in differentiating TT from BT.[15]

In BL, granuloma rich in foamy histiocytes and few epithelioid cells are seen and LL characterized by diffuse sheets of foamy histiocytes with Grenz zone.[16] In BB, the macrophages are uniformly activated to epithelioid cells but distinct granulomas and lymphocytes are scanty. Dermal edema will be prominent between inflammatory cells.

In indeterminate leprosy, there is mild lymphocytic infiltration around neurovascular bundles, sweat glands and erector pili muscle. No formed epithelioid cell granulomas are observed.[17]

Both clinically and histopathologically, the most common diagnosis in this study was borderline tuberculoid leprosy similar to many studies published in literature. In a study of Kumar et al, out of 372 cases, 269 (72.31%) were BT.[18] In a study of Bal A et al, out of 303 leprosy cases, 206 was BT.[17] Manandhar U et al studied 75 cases in which 30 (40%) cases were BT histologically.[19] Kumar et al in 2000, found clinicopathological correlation in 60.6% of cases and Rizvi et al in 2015 in 70% cases.[18,20] Pandya et al study showed the least concordance with 58%.[21] In our study, it was slightly higher 79.44% (Table 4). The data of present study and other comparative studies suggest that correlation in the polar group was maximum and was seen in Lepromatous leprosy which because of their stability showed a consistent histopathology.[22] Our study is quite similar to Mathur et al study. overall coincidence of clinical and histopathological diagnoses of classification was seen in 80.4% of cases. The maximum correlation (95.2%) was noted in LL patients.[23] The cell mediated immune response and bacterial load is determined by bacteriological index.

However the diagnosis cannot be made only on the basis of bacteriological index as it can vary in various type of leprosy.[24] In present study, acid-fast bacilli was seen in all BL and LL cases. High Bacteriological index (5+-6+) was seen in LL. Tuberculoid and borderline tuberculoid leprosy(TT-BT) often overlap clinically, histologically and immunologically but differ only in degree and similarly, borderline lepromatous and lepromatous leprosy(BL-LL). Therefore, combining these two groups does not affect the chemotherapy and outcome of the disease. The disparity between clinical and histological observations was anticipated because the parameters used for the histopathologic classification are well-defined, specific 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.[25] Singh et al, Clinical comparative study of Ridley-Jopling and WHO classification suggest high concordance rate (85.6%) for WHO classification compared to Ridley-Jopling (58.6%) and highlights the importance of histopathological examination for exact typing of leprosy in instituting the proper therapy so as to prevent the undesirable complications.[26]

Conclusion

Clinical classification of early lesions of leprosy is often difficult. Clinical correlation of late lesions of leprosy is significantly good probably due to more specific and stable histopathological feature. The concordance was high in LL. BB is rarely diagnosed, Indeterminate leprosy is frequently diagnosed both clinically and histopathologically. There can be overlap between different types of leprosy, both clinically and morphologically. So correlation of clinical and histopathological features along with bacteriological index appears to be more useful for accurate typing of leprosy.

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