ORIGINAL ARTICLE

Clinico-Histopathological Correlation in Leprosy

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Abstract

Clinical diagnosis of early leprosy lesions poses difficulties. The present study was carried to correlate histological diagnosis of skin biopsies of untreated leprosy cases with clinical diagnosis using Ridley-Jopling classification. 270 skin biopsies of untreated leprosy cases over a period of two years were included . Paraffin sections of biopsies were stained with Hematoxylin & Eosin, Ziehl-Neelsen's & Fite's stains, examined and classified histopathologically according to Ridley- Jopling scale and then correlated with clinical diagnosis. Overall concordance of clinical and histopathological diagnosis was seen in 53.44% cases with maximum parity in lepromatous leprosy (75.86%), followed by borderline lepromatous (58.82%), borderline tuberculoid (53.01%), tuberculoid (47.37%), and least in mid-borderline cases (37.35%). Indeterminate leprosy cases showed 100% clinicopathological concordance. There was minor disagreement (difference of one group) in 29.56% and major disagreement (difference of two or more groups) in 17% cases. We noted minor disagreement in polar leprosy (TT+LL) and major discordance in borderline group (BT+BB+BL). Cases in borderline group are in continuously changing immunological spectrum and histological classification because of its definitve features gives a better indication than clinical classification for any recent shift of a case in the spectrum. Skin biopsy may be studied in all cases of leprosy for better diagnosis.

Key Words

Leprosy, Ridley-Jopling Classification, Histopathology

Introduction

Leprosy, also known as Hansen's disease, is a chronic, infectious disease that primarily affects the skin and the peripheral nerves (1). It is a growing endemic (2) as its elimination is not as straightforward as it seemed (3). Leprosy expresses itself in different clinico-pathological forms depending on the immune status of the host (4,5) Diagnosis of leprosy is based on different clinical parameters which involves detailed examination of skin lesions and peripheral nerves (6) Demonstration of acid –fast bacilli in slit skin smears by Ziehl- Neelsen's staining also aids in diagnosis of leprosy (7) A reliable diagnosis hinges around a good histopathological diagnosis and demonstration of bacilli in histopathological sections (8,9) Modified Fite's procedure has proved most valuable in demonstrating lepra bacilli in tissue sections (10). Clinical classification gives recognition only to gross appearances of the lesions, while the parameters used for the histopathological classification are well defined, precise and also take into account the immunological manifestations which enable it to successfully bridge the pitfalls in leprosy diagnosis.Histopathology provides confirmatory information for suspect cases which can be missed in clinical practice or epidemiological studies and helps in exact typing. Histology also gives indication of progression and regression of disease under treatment (11) Ridley and Jopling were the first to suggest a subdivision of leprosy on an immunological basis into five types; tuberculoid (TT), borderline tuberculoid (BT), mid-

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borderline (BB), borderline lepromatous (BL) & lepromatous (LL) (12) Later they further developed this idea and correlated clinical and bacteriological findings in each group with respective immunological and histological findings (6). Classification of leprosy is essential primarily for the purpose of communication at different levels and can be adjudged as satisfactory only if it can be applied without much difficulty by different groups of workers i.e. clinicians, pathologists or immunologists. The present study was carried out to assess the concordance between clinical and histopathological diagnosis in cases of leprosy using Ridley- Jopling scale.

Material & Methods

The study was carried out on the skin biopsies from untreated cases of leprosy seen in the Department of Dermatology and reported in the histopathology section of the Department of Pathology, Government Medical College, Jammu between Nov 1, 2003 to Oct 31, 2006. Hematoxylin and Eosin stained sections (13) of skin biopsies of all the cases of leprosy were examined for:-

a) Epidermal atrophy, epithelioid granulomas, number & distribution of lymphocytes, histiocytes & foam cells.
b) Infiltration of nerves, blood vessels and adnexa.
c) Grenz zone.

Sections stained with Ziehl Neelsen's stain (13) and Modified Fite's stain (10) were examined for lepra bacilli in all cases. Histopathological findings were graded into (TT), (BT), (BB), (BL) and (LL) according to Ridley and Jopling scale (6). Sections showing scattered non-specific lympho-histiocytic infiltration with cellular reaction with in dermal nerve or presence of bacilli in subepidermal zone/ arrectores pilorum muscle/ dermal nerve were classified as indeterminate leprosy (14) and also included for purpose of analysis. Biopsies which did not include the full depth of dermis together with a portion of subcutaneous fat were considered as inadequate and not classified histopathologically.

Clinical diagnosis of the leprosy cases (as provided by department of Dermatology) using Ridley & Jopling scale was correlated with the results of histopathologic examinaton of their respective biopsies. Cases with inadequate biopsies and biopsies which did not reveal histology of the leprosy (non specific) or showing features of reactional leprosy were excluded from clinico-histopathological correlation.

Results

This study was done on skin biopsies of 270 clinically diagnosed untreated cases of leprosy of which 234 were males and 36 were females. Their age ranged from 8 to 78 years with the majority of them in the age group of 20-40 years. Histopathological features of leprosy were observed only in biopsies of 247 cases (Table-1), while other cases which showed histological features of non specific dermatitis (9), reactional leprosy(4) or with inadequate.biopsy(10) were excluded from clinico histopathological correlation. The distribution of 247 cases on the clinical leprosy spectrum based on Ridley-Jopling scale revealed maximum cases (74.09%) in borderline group (BT+BB+BL). In polar groups, 19 (7.69%) cases belonged to TT and 29 (11.74%) to LL (Table-2). Least number (6.48%) of cases were classified as indeterminate leprosy (IL).Maximum clinico-histopathological correlation was seen in IL (100%) followed by LL (75.86%), BL (58.82%), BT (53.01%), TT (47.37%) and minimum in BB (37.35%) as shown in table-2. Overall concordance of diagnosis was seen in 53.44% cases. When cases of BT, BB and BL were clubbed together as one intermediate borderline group between two polar forms for clinical and histological diagnosis, the high parity of 71.59% was observed. However, when we considered TT and BT together as one group, and also BL and LL together as other group, clinico-histopathological concordance was 71.57% for the TT-BT group and 89.13% for BL-LL group. On correlating clinical diagnosis with histological diagnosis only minor disagreement (difference of one group) was observed in TT and LL cases with exception of one case of LL showing major disagreement (difference of two or more groups) while no disagreement in clinical and histological diagnosis was noted in clinically diagnosed cases of indeterminate leprosy (Table-3). However major disagreement was seen in borderline spectrum ranging from17.56% to 25.3%.

Table-1 Histological Type of Leprosy

Histological Type	No	% age
TT	20	7.41%
BT	87	32.22%
BB	45	16.67%
BL	16	5.93%
LL	25	9.26%
IL	54	20%
Leprosy in Reaction	4	1.48%
NSD	9	3.33%
Inadequate Biopsy	10	3.7%
Total	270	100%

Table-2 Clinico-Histopathological Correlation

Clinical Diagnosis	Histopathological Diagnosis						Parity % age
	TT	BT	BB	BL	LL	IL	
TT (19)	9	10					47.37%
BT (83)	10	44	12			17	53.01%
BB (83)	1	31	31			20	37.35%
BL (17)		2	1	10	3	1	58.82%
LL (29)			1	6	22		75.86%
IL (16)						16	100%
Total (247)	20	87	45	16	25	54	53.44%

TT-Tuberculoid, BT-Borderline Tuberculoid, BB-Mid Borderline, BL-Borderline Lepromatous, LL- Lepromatous, IL- Indeterminate

Table-3 Disagreement in Clinical and Histopathological Diagnosis

Clinical Cases		Complete Parity	Minor Disagreement	Major Disagreement
Type	No.	No. % age	No.% age	No.% age
TT	19	9 (47.37%)	10 (52.6%)	
BT	83	44 (53.01%)	22 (26.5%)	17(20.48%)
BB	83	31(37.35%)	31 (37.35%)	21(25.3%)
BL	17	10 (58.82%)	4 (23.53%)	3 (17.65%)
LL	29	22 (75.86%)	6 (20.69%)	1 (3.45%)
IL	16	16 (100%)		
Total	247	132(53.44%)	73(29.56%)	42(17.0%)

TT-Tuberculoid, BT-Borderline Tuberculoid, BB-Mid Borderline, BL-Borderline Lepromatous, LL- Lepromatous, IL- Inteermeediate

Discussion

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 (6) which is primarily based on immunity but has been correlated with clinical, histopathological and bacteriological findings. Despite having such an accurate classification, leprosy cases showed so many diversities between the clinical and histopathological features. Clinical spectrum of leprosy cases in the present study revealed maximum cases (74.09%) in borderline group (BT+BB+BL), followed by LL(11.74%), TT(7.69%) and least in IL group (6.48%) and similar predominance of cases in borderline group was also observed by Shenoi & Sidappa(15), Nadkarni & Rege(16) and Moorthy *et al* (17) In the present study the histopathological characteristics were consistent with the clinical diagnosis in 132 out of 247(53.44%) cases. After excluding indeterminate cases in this study, lepromatous cases seem to present the least problem for classification (Table-2). Similar highest percentage of agreement between clinical and histopathological diagnoses of lepromatous leprosy cases is also observed by Shenoi& Sidappa (15), Pandey & Tailor (18), Bhatia *et al* (19), Kalla *et al* (20) and Shanker Naryan *et al* (21) in their respective studies. Least agreement was seen in cases of mid borderline leprosy in this study, which is in concordance to the observations recorded by Shenoi & Siddappa(15), Nadkarni & Rege(16), , Moorthy *et al* (17), Bhatia *et al* (19), Kalla *et al* (20), Shankar Naryan *et al* (21) and Singhi *et al*(22) Maximum major disagreement (25.3%) between clinical and histopathological diagnosis was observed in midborderline cases of present study and same was also noted by Singhi *et al* (20) Midborderline leprosy is immunologically the least stable and variety of clinical lesions of different morphology may be found in the same patient. It is therefore necessary to relate the histological features with the clinical characteristics presented by the particular morpholgical lesion subjected to biopsy. If this is done carefully, it may be possible to achieve a better correlation of clinical with the histological changes.

When we combined TT and BT cases in one tuberculoid group and LL and BL cases in single lepromatous group for the purpose of analysis, we noted

better clinico-histopathological correlation. Similar rise in clinico-histopathological concordance of tuberculoid group and lepromatous group was also noted by Bhatia *et al* (19) Tuberculoid and borderline tuberculoid leprosy often overlap clinically, histologically and immunologically but differ only in degree and same is true for borderline lepromatous and lepromatous leprosy. Therefore, combining these two groups (TT-BT and BL-LL) does not affect the chemotherapy and outcome of the disease.

In the present study, 20% cases were diagnosed as indeterminate leprosy histopathologically as against 6.48% cases clinically. Nadkarni & Rege (16) had also diagnosed sizeable proportion (15.9%) of the cases as indeterminate histopathologically, who were clinically classified as cases of TT, BT, BB or BL leprosy. Indeterminate lesion is one which cannot be classified with in the Ridley-Jopling spectrum due to lack of distinguishing features, and this happens more often histologically (due to failure to find a granuloma) than clinically. In the present study the high percentage of "indeterminate" leprosy noted histologically in clinical BT - BB range and low percentage in BL group could have been due to immunological difference in the host responses.

The disparity between clinical and histological observations was anticipated because the parameters used for the histopathologic classification are well-defined, precise 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. Moreover, a sizable proportion of leprosy cases (BT+BB+BL) are in a continuously changing immunological spectrum and histological classification gives a better indication for any recent shift of a case position in the spectrum. In some early cases, clinical signs and symptoms may precede the presently known characteristic tissue changes, or vice versa(19). If a biopsy is taken at an early stage, there is likely to be discordance between the clinical and histopathologic observations. As disparity depends upon the lesion biopsied at the time of study, biopsy from the lesion which is morphologically suggestive of clinical diagnosis, serial biopsies from the same lesion, or from paired lesions, should be studied for a better clinico-histopathological correlation.

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