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Clinicohistopathological Correlation of Leprosy in A Peripheral Hospital of Mumbai.

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ABSTRACT

Background *-Leprosy a chronic infectious disease involving mainly skin and peripheral nerves presents with different clinicopathological forms.*

Aim *-To correlate clinical and histological diagnosis of skin biopsies of leprosy using Ridley- Jopling classification*

Material and Methods *- A prospective study was done on 54 cases of leprosy over a period of 2 years. Skin biopsies were studied for different histological features and fite stain was done to classify different types of leprosy .Clinicohistopathological Concordance rate was calculated .*

Result *-In 54 cases of leprosy studied,we observed clinicohistopathological concordance was maximum in ENL(100%) followed by BT(58.2%), BL(50%), Lepra Reaction 1(50%),Histioid leprosy(50%), TT(44.44%), and least in IL(28.57%). Overall, it was 51.85%.*

Conclusion *-Leprosy which is a major health problem in India can be reduced with the help of simple and important tool of histological and bacteriological examination for lepra bacilli , of skin biopsy and a good clinicopathological correlation .*

KEYWORDS : Leprosy, Skin Biopsy, Histology

INTRODUCTION

Leprosy is one of the major public health problems of the developing countries including India.[1] It is a progressive, chronic granulomatous infection caused by Mycobacterium leprae. Leprosy-primarily affects the skin and peripheral nerves ,but certain other tissues like the mucosa of the upper respiratory tract,the reticuloendothelial system the testes and the eyes are also affected.[2] Leprosy expresses itself in different clinico-pathological forms depending on the immune status of the hostB. Ridley and Jopling suggested a subdivision of leprosy based on clinical,histological,microbiological and immunological criterea into five types: Tuberculoid -TT, Borderline Tuberculoid -BT, Mid borderline (BB), Borderline Lepromatous-BL & Lepromatous -LL (F).Diagnosis of leprosy depends upon the clinical examination of skin lesions and peripheral nerves, demonstration of acid fast baclilli on split skin smear and demonstration of its characteristic histopathological features on biopsy[3].However due to its clinical diversity as well as its ability to mimic other diseases ,sometimes leprosy is difficult to diagnose clinically. In such cases clinico histopathological correlation is necessary to arrive at a correct diagnosis for the optimum treatment of the patients.[4] The present study was undertaken to demonstrate the use of clinical and histopathological correlation of skin biopsy to arrive at a definitive diagnosis and to classify the different types of leprosy using the Ridley Jopling scale.-

MATERIAL AND METHODS

A prospective study was conducted on 54 clinically diagnosed cases of leprosy in th department of pathology at DR R. N. Cooper Hospital, for a period of 2 years between January 2012 till December 2013. Permission of ethics committee was obtained. Patients already taking treatment were excluded from the study.

Punch biopsies of clinically suspected cases of leprosy were received from the dermatology department and fixed in 10% buffered formalin , processed and stained with hematoxylin and eosin (HE) and Fite Faraco stain. History and clinical details of patients pertaining to clinical diagnosis, location of skin lesion, site of biopsy ,type of skin lesion were recorded. Histopathological classification of leprosy was done according to Ridley and Jopling classification and bacteriological index was given as per Ridley's Logarithmic Scale. 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. A clinicopathological concordance was done on all the cases.Statistical Analysis was done using SPSS 15 software. Percentages were calculated for the various categories.

RESULTS

The present study was done on 54 cases of skin biopsies diagnosed clinically as leprosy. Out of these cases (Table-2) borderline tuberculoid leprosy (BT)(31.4%) constituted the most common subtype followed by tuberculoid leprosy,(TL)(16.67%) borderline lepromatous leprosy(BL)(11.11%) indeterminate leprosy,(12.96%) histoid leprosy(11.11%) and lepromatous leprosy(5.56%). Reactions constituted 11% of the cases with 4 cases of erythema nodosum leprosum (ENL) and 2 cases of type 1 reaction.Maximum number of cases were in the age group of 21 to 30 years followed by 31 to 40 years.-The sex distribution pattern of leprosy showed a male preponderance of 43males(79.63 %) as compared to 11(20.37%) females. Upper limb (18 cases) was the most common site involved followed by trunk(14 cases) and face(6 cases).Multiple site of involvement (12 cases) was seen in lepromatous leprosy and histoid leprosy. Clinical presentation in 15 cases of leprosy was in the form of hypopigmented ,hypoanaesthetic patch, whereas 39 cases of leprosy presented as an erythematous plaque/papule/ nodule.The histopathological features of the different types of leprosy were as follows. Cases showing granulomas having fewer lymphocytes and more number of giant cells & not encroaching upon epidermis were classified as borderline tuberculoid leprosy. Biopsies with well formed epithelioid granulomas with rim of lymphocytes distributed throughout the dermis especially around adnexal structures and neurovascular bundles and encroaching upon basal layer of epidermis were classified as tuberculoid leprosy. Cases diagnosed as borderline lepromatous leprosy ,revealed sheets of foamy cells admixed with few lymphocytes, illformed epithelioid granulomas and presence of grenz zone.Cases of lepromatous leprosy showed presence of sheets of foamy cells, lack of epithelioid granuloma and presence of grenz zone .

Histioid leprosy on skin biopsies showed thinning of epidermis with presence of a nodule in upper dermis composed of sheets of modified macrophages in spindle form with presence of Grenz zone. Cases with periadnexal and perineurovascular chronic inflammatory cells but no definite granuloma formation were categorized as indeterminate leprosy. One(1.8%) case each of borderline tuberculoid and tuberculoid leprosy showed dermal oedema ,inflammatory infiltrate and vasculitis and were categorised as Type 1 lepra reaction. Cases of leprosy diagnosed as erythema nodosum leprosum (ENL) showed dense inflammatory infiltrate in the dermis and subcutaneous fat along with vasculitis. One case of tuberculoid leprosy was clinically

diagnosed as lupus vulgaris. Fite stain was positive in 18 out of 54 cases(33.33%). We found that one case each of tuberculoid leprosy and indeterminate leprosy showed positivity for lepra bacilli whereas 4 out of 6 cases of borderline lepromatous leprosy , all 3 cases of lepromatous leprosy and all 6 cases of histoid leprosy were fite positive. Lepra bacilli were demonstrated in 2 cases of borderline tuberculoid and in one case of ENL. However we did not find lepra bacilli in any case of type 1 lepra reaction.The clinicopathological concordance of leprosy in our study was 44.44% for TT,58.82% for BT,50% for BL,33.33% for LL,28.57% for indeterminate type,50% for histoid type,100% in cases of ENL and 50% in cases of type I reaction.The overall concordance rate was 51.8%.

DISCUSSION

Leprosy is widely prevalent in India including cosmopolitan cities like Mumbai.There were 0.83 lakh leprosy cases reported in 2011 with prevalence rate of 0.69 per 10000 population.[5]Leprosy presents as a wide clinicopathological spectrum depending upon the immunity of the patient.[5]Moreover in the same patient there can be a change in the different subtypes with changing immune status. Though in many cases the diagnosis is based purely on clinical and microbiological studies , in doubtful cases biopsy is necessary for subclassification of various types of leprosy. Moreover correct labeling of paucibacillary and multibacillary cases is a prerequisite to design treatment protocol. Hence clinicopathological correlation assumes a pivotal role for early diagnosis and proper labeling of a case.[1] We analysed 54 cases of leprosy on the basis of most commonly accepted classification of Ridley and Jopling .In our study Borderline tuberculoid leprosy (BT) (31.4%) constituted the most common subtype followed by tuberculoid leprosy.(TL)(16.67%). Similar findings have been reported by Grover et al[7] from Mumbai, Bal et al [8] from Punjab and Gautam et al [9] from Nepal while lepromatous leprosy(LL) has been found to be more common as reported by Jindal from Himachal Pradesh [13].Hence a regional variation is observed in different types of leprosy across the country. Thus we can conclude that leprosy subtypes BT and TT are more common in this population of Mumbai . Maximum patients were in the age group of 21 to 30 years which is similar to study done by Mathur et al.[2] The sex distribution pattern of leprosy revealed a male preponderance of 43 males as compared to 11 females with a male female ratio of 3.9:1.Grover [7] and Jayalaxmi [11] have also found a male preponderance with 79.42% and 65% male leprosy patients. This may be due to more hospital access to males as compared to females due to socioeconomic factors. In our study upper limb(33.33%) was the most common site followed by trunk(22.22%) and face (11.11%).Multiple sites were more common in lepromatous and histoid leprosy. Similarly Grover et al has also reported upper limb to be the commonest site with 29% cases [7] while Jha et al has found neck to be the common site[10]. In our study we also studied the clinical presentation of various type of leprosy. The commonest clinical presentation was in the form of erythematous plaque/papule/nodule with 39 cases while 15 patients presented with hypopigmented, hypoanaesthetic patches. We observed that cases of histioid leprosy, lepromatous leprosy and ENL mainly presented with nodules . However presentation of borderline leprosy was in the form of erythematous plaque. Thus patients presenting with hypopigmented patch, were towards tuberculoid pole of leprosy and patients towards lepromatous pole presented with erythematous plaques,or nodules .Giridhar et al [5] observed in their study that leprosy more commonly presented with hypopigmented patch with 68 (69.4%) cases than as erythematous plaques with 30 (30.6%) cases which was not the case in our study. In our study , we demonstrated lepra bacilli in 18 out of 54 cases of leprosy on fite faraco stain Thus we obtained 33.33% fite positivity in our study, whereas Giridhar et al [5] demonstrated 56.12% fite positivity in their study. Bal et al [8] found fite positivity in 136 out of 373 cases(36.4%)which was comparable with our study.The clinico pathological concordance was seen in 51.85% of our cases. Cases of ENL showed maximum percentage of clinicopathological concordance with all 4 cases diagnosed as ENL both clinically as well as histopathologically. We diagnosed 9 cases as borderline tuberculoid leprosy showing 58.82% clinicopathological concordance . The histopathological characteristics were consistent with the clinical diagnosis in 3 cases of borderline lepromatous(BL) , 1 case of type 1 Lepra reaction,1 case of histioid leprosy, thus all were showing 50% concordance.In our study We observed 44.44% concordance in tuberculoid leprosy where 3 cases were diagnosed as tuberculoid leprosy clinically as well as histologically .We observed least concordance (28.57%) in indeterminate leprosy.Hence maximum discordance was seen in cases of indeterminate type where the histological features are non specific and in the tuberculoid pole where BT and TT can showed overlapping features.

Ridley and Jopling reported clinicopathological concordance to be 68.3%, [6] Anuja et al has reported it to be 53.44% [3] and Giridhar et al as 60.23% [5]. Chaudhari B., Mehta R.P. [12] carried out a study of 126 clinically diagnosed cases of leprosy They found maximum clinico-histopathological correlation in TT (86.21%) followed by LL (83.33%), BL (63.33%), BT (50%) and minimum in BB (28.57%) Overall concordance of diagnosis was seen in 70.83% cases. Anuja et al [3] studty shows 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%).[3] M Giridhar et al studied clinicohistopathological concordance in 100 cases of Leprosy [5] . An overall clinicohistopathological concordance in this study was 60.23%, 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%).

The discordance between clinical and histopathological diagnosis was noticed because of various factors ,histopathological diagnosis, including different criteria used to select the cases, number of cases of each type, age of the lesion, nature and depth of the biopsy, quality of the section, number of acid-fast stained sections examined, immunological and treatment status of the patient at the time of diagnosis. If biopsy is taken at an early stage, discordance between clinical and histopathologic observation is more likely. There is also inter observer variation both clinically and histopathologically, so there could be overlap between different types of leprosy. Clinician must know proper selection of site and type of lesion for histological examination.[6]

CONCLUSION

The high incidence of leprosy which is a major health problem in India can be reduced with the help of early diagnosis and prompt treatment. Early diagnosis can be aided by histological and bacteriological examination of a properly biopsied skin lesion .A good clinicopathological correlation is mandatory as there is overlap in histopathologic features of different types of leprosy and morphology alone is not specific in all cases. This is useful for the accurate classification of leprosy, proper treatment and to prevent undesirable complications of leprosy.

Tables

Table No 1: Clinicopathological concordance of various types of leprosy in present study

Final Diagnosis	Clinical types									
	TT	BT	BL	LL	Lupus Vulgaris	Histoid Leprosy	ENL	TYPE I Lepra reaction	Indeterminate leprosy	Percentage (%)of concordance
TT (9)	4	4	00	0	01	00	00	00	00	44.44%
BT (17)	1	10	01	01	00	00	00	02	02	58.82%
BL(06)	0	01	03	01	00	00	01	00	00	50 .00%
LL (03)	0	01	00	01	00	01	00	00	00	33.33%
Indeterminate leprosy (07)	1	04	00	00	00	00	00	00	02	28.57%
Histoid Leprosy(06)	1	01	00	00	00	03	01	00	00	50.00%
ENL (04)	0	00	00	00	00	00	04	00	00	100 %
TYPE I Lepra reaction(02)	0	00	00	01	00	00	00	01	00	50.00%
TOTAL (54)	6	20	04	04	01	04	06	03	06	

Table No 2: Clinical presentation in various types leprosy in present study

Final diagnosis	Hypopigmented patch(no. of cases)	Erythematous plaque /papule /nodule (no of cases)	Total no of cases
1.Tuberculoid leprosy	02	07	09
2.Boderline tuberculoid	06	11	17
3.Boderline lepromatous	01	05	06
4 lepromatous leprosy	01	02	03
5.Indeterminate leprosy	05	02	07
6. Histoid Leprosy	00	06	06
7. ENL	00	04	04
8.TYPE I Lepra reaction	00	02	02
Total	15	39	54

Clinicohistopathological study of leprosy in a peripheral Hospital of Mumbai.

FIGURES-

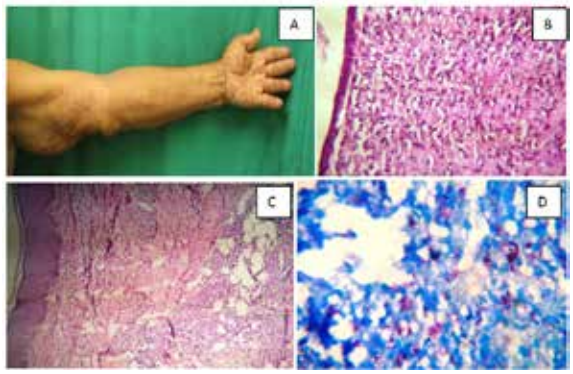
Figure 1-

(A) Borderline Tuberculoid Leprosy (BT)shows a single plaque over arm, well defined at places and ill defined at other place, showing atrophy and erythema. **(B)** BT showing confluent granuloma seen in upper & mid dermis with giant cells.(100x) **(C)**Tuberculoid lepromatous leprosy shows a well defined plaque having an erythematous infiltrated margin and atrophy at the center. **(D)** TL showing epithelioid granuloma encroaching the epidermis along with perineural involvement. (100X)

Figure 2-

(A) Borderline Lepromatous Leprosy shows bilateral symmetrical hypopigmented plaques on the back. (B) BL showing Grenz zone with mixtureof epithelioid cells & foamy cells in the upper & mid dermis.(100X) **(C)**Lepromatous leprosy showing infiltrations of pinna and cheek by LL lesions . **(D)** Lepromatous leprosy with sheets of foamy Lepra cells in the dermis. (100X)

Figure 3 –



(A) Histoid leprosy shows many discrete skin coloured nodules on the upper arm. **(B)**Histopathology of histioid Leprosy showing sheets of spindle cells in upper dermis.(400X)
(C) ENL showing perivascular inflammatory infiltrate along with involvement of subcutaneous tissue. (100X) **(D)**LL showing numerous acid fast bacilli, some within lepra cells.(1000X)

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