

A histopathological study and clinico histopathological correlation of single lesions in leprosy

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Abstract

Background: Leprosy caused by Mycobacterium Leprae is an important public health concern. Single lesions in leprosy are commonly seen in TT, BT and indeterminate leprosy. **Aim:** The aim of the present study is to evaluate histopathological features of single lesions in different clinical types of leprosy and evaluate clinico histopathological correlation. **Methods:** Scalpel biopsies of single leprosy lesions from all 40 patients were done followed by staining of slides with Haemotoxilin and Eosin stains. A thorough study of histopathological features of slides was done followed clinico- histopathological correlation. **Results:** There were 7 cases of indeterminate leprosy, 27 cases of BT type and 6 cases of TT type clinically. There were clinico- histopathological correlations in 32.5% of the total cases. More clinico histopathological correlation was seen among TT type and least correlation was seen among BT type. **Conclusion:** There is clinico histopathological correlation in 32.5% of the total cases. More correlation is seen TT type of leprosy than in BT type of leprosy in single lesions.

Key words: Leprosy, Single lesion, Indeterminate, Borderline Tuberculoid, Tuberculoid.

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Introduction

Leprosy is a disease of great antiquity. It is a chronic granulomatous infection caused by obligate intracellular organism. M. Lepra [1]. Infectious in some cases are affecting the peripheral nervous system, the skin and certain other tissues [2]. Although prevalence has decreased, the incidence remains relatively static [3]. Leprosy presents an unparalleled challenge to the sociologist, the bacteriologist, the pathologist, the epidermologist the pharmacologist and practitioner of medicine [4]. Based on clinical, immunological histopathological and bacteriological. parameters leprosy is classified. lepromatous leprosy, borderline lepromatous, borderline- borderline, borderline tuberculoid and tuberculoid leprosy [5]. Single lesions are commonly seen in a wide variety of clinical leprosy. Single lesions which may reflect integrity of the host immunity to the disease are seen commonly in TT and BT and indeterminate leprosy. They have been reported in lepromatous leprosy (subpolar) also. The present study attempts at the detailed

detailed histopathological examination and clinico histopathological correlation of single lesions in leprosy.

Methods

The study is conducted in department of Dermatology, Mahatma Gandhi Memorial Hospital Warangal over a period of 18 months and is approved by research ethical committee. A detailed clinical history was recorded followed by thorough clinical examination of the patients. Children below 5 years patients, patients on antileprotic treatment, pregnant woman and patients on corticosteroid therapy were excluded. In all cases routine haematology and other laboratory investigations were done. Chest x-rays were taken in all cases. Lepromin test was not done as the facility was not available in this institute. Written consent was obtained from all the 40 patients who were subjected to histopathological examination. Scalpel biopsies were taken from the area of the lesion in the vicinity of the margin. Histopathology sections were stained with hematoxylin and eosin stain and were examined in details for histopathological changes. Fite - faraco

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staining was not done as the facility was not available in this institute. Ridley & Jopling classification was used

for clinical and histopathological diagnosis of the single lesions in leprosy.

Results

The present study included 40 leprosy patients with single lesions. There were 29 males and 11 females with male female ratio of 2.63:1. Common age affected was 11 to 60 years. The percentage single lesions among total leprosy patients were 12.5 %. Clinically there were 7 cases of indeterminate leprosy, 27 cases of borderline tuberculoid leprosy and 6 cases of tuberculoid leprosy. Histopathological changes were noted in all cases as recorded below.

Histopathology of Epidermal changes: Epidermal changes were recorded in almost all cases. The most common change seen in epidermis was hypertrophy with alternative areas of atrophy (focal atrophy) (Table 1).

Table 1: Histopathology of epidermis

	TT	IND	BT
No Change	-	1	-
Slight strophy	-	1	9
Epithelial hyper - plasis	1	3	3
Hypertrophy with atrophy	5	2	15
Spogiosis	1	1	3

In TT group epithelial hyperplasia was present in 1 case (2.5%). Hypertrophy with areas of atrophy was seen in 5 cases (12.5%). In indeterminate group epithelium was normal in 1 case (2.5%). Atrophy of epithelium was present in 1 case (2.5%). Epithelial of hyperplasia was present in 3 cases (7.5%) hypertrophy with atrophy was present in 2 cases (5%). In BT group atrophy of epithelium was present in 9 cases (22.5%) epithelial hyperplasia was present in 3 cases (7.5%). Hypertrophy with atrophy of epithelium was seen 15 cases (37.5%). Spongiosis is seen in 3 cases (7.5%).

Histopathology of Dermal changes: Infiltration of dermis was seen in majority of cases. The infiltrate was seen occupying upper dermis. Only one case did not show any sort of infiltration in the dermis.

Infiltrate Cells: Lymphocytes, macrophages and epitheloid cells were predominantly seen. Mononuclear cells were seen in 10 cases. Neutrophils were not observed in any of these cases.

Skin Appendages: Lesions of appendages such as atrophy and disorganization of arrector pill were noted. The most common change seen was infiltration of sweat glands and hair follicles with lymphocytes and mononuclear cells in some cases. (Table 2)

Table 2: Histopathological features of appendages

	BT cases	IND Cases	TT Cases
Arrector Pili Muscle			
No changes	7	1	
Inflammatory infiltration	15	3	6
Attrpohy	5	3	
Sweat Glands			
No change	6	4	
Inflammatory infiltration	19	3	6
Not demonstrable	2		
Hair Follicles			
No change	6	4	
Inflammation	19	3	6
Attrpohy	2		

The infiltration around the sweat gland was of a lower degree compared to the infiltration around the arrector pilorum. In clinically indeterminate group arrector pili were normal in 1 case. Inflammatory changes were present in 3 cases and there was atrophy in 3 cases. In BT group arrector pili were normal in 7 cases while in 15 cases there were inflammatory changes. There was atrophy of the muscle in the remaining 5 cases. In TT group all the 6 cases showed inflammatory changes in arrector pili muscles.

Sweat Glands: In indeterminate group sweat glands and hair follicles were normal in 4 cases while inflammatory changes were seen 3 cases. In BT group inflammatory changes were seen 19 cases (47.5%) while no changes were observed in 6 (15%) cases. Sweat glands and hair follicles were not demonstrable in 2(5%) cases in this group. In TT group inflammatory changes in sweat glands and hair follicles were seen in all the 6 cases (15%).

Histopathology of Cutaneous Nerves: Small cutaneous nerves in the deep dermis exhibited some changes. The most common change (Table 3) was lymphocytic infiltration around the perineurium.

Table 3: Histopathology of cutaneous nerves

	Number of cases		
	Indeter	BTs	TTs
No change	3	7	0
Perineural	4	16	6
Infiltration within the nerve	0	0	0
Not demonstrable.	0	4	0

In indeterminate group perineural infiltration was seen 4 (10%) cases and no changes were seen in 3 cases. In TT group all the 6 cases showed inflammatory changes. In BT group nerves were normal in 7 cases (17.5%). Perineural inflammation was present in 16 cases (40%) while nerves were not demonstrable in 4 cases. Of the 40 cases in the present study overall clinico histopathological correlation was present in 13 cases accounting for 32.5%. Within the indeterminate group of 7 cases clinico – histopathological correlation was present in 4 cases. (57.14%) Among tuberculoid type clinico histopathological correlation was present in 5 out of 6 cases (83.13%). In BT group the correlation was present in only 4 cases (14.81%). Thus there is 85.19% lack of correlation in this group.

Discussion

Histopathological Study: In the present study of 40 cases all the patients were subjected to histopathological study. The skin biopsies (scalpel biopsy) were taken from the margin of the lesion.

Histopathological findings in the 40 patients under the present study divided into three categories.

- 1) Clinically indeterminate lesions.
- 2) Clinically borderline tuberculoid lesions.
- 3) Clinically tuberculoid lesions.

Histopathological findings of indeterminate (clinical) lesions

Epidermis: Hypertrophy alternating with areas of atrophy was found in 2 cases. Epithelial hyperplasia was noted in 3 cases. Atrophy of the epithelium was

noted in 1 case while the remaining 1 case did not show any significant changes in epithelium. Spongiosis was noted in one case. US Agarwal et al noted focal atrophy

of epidermis in majority of cases (7/9) cases) in indeterminate lesions [6]. Liu- et al reported no changes in epithelium in 75% of cases [7], spongiosis in 10% and atrophy of epithelium in 5%. Epithelial hyperplasia was seen in none of his cases.

Dermis: Dermis, especially upper dermis showed infiltration with lymphocytes and monocytes. Rarely macrophages were also seen in the infiltrates. Similar observation were made in earlier studies [6, 7].

Skin Appendages: Atrophy of arrector pili muscles was observed in 3 cases. Inflammatory changes of arrector pili were observed in 3 cases (42.85%). No changes were seen in 1 case (14.27%).

Liu et al reported no changes in arrector pili muscles in 53% of cases, inflammatory changes in 41% of patients and atrophy in 6%) of cases [7].

Sweat Glands: Inflammatory infiltrate was seen in 3 cases (42.85%) and no changes were seen in 4 cases (57.12%).

Hair Follicles and Sebaceous Glands: Inflammatory changes were seen in 3 patients (42.85%) and no changes were seen in 4 cases (57.12%). In the literature changes were seen in 28% of patients [7].

Nerves: Perineural infiltration predominantly with lymphocytes was seen 4 patients (57.12%) while no neural changes were seen in 3 cases (42.85%) Liu et al observed perineural changes in 94% of indeterminate lesions.

Considering the histopathological criteria for diagnosis of indeterminate leprosy 4 of the 7 indeterminate lesions (clinically) in the present study are consistent histo – pathologically with the clinical diagnosis (57.12%). The remaining three cases (42.85%) were diagnosed as non specific dermatitis.

The histopathological changes seen in the epidermis of indeterminate lesions on the exposed parts of body in majority of cases probably is consistent with hypothesis that single leprosy lesions reflect sites of entry of *M. Lepras* through skin via wounds and abrasions. It was remarked that such a distribution of lesions could be satisfactory explained by assuming a portal of entry other than skin, with a tendency of localization of infection whenever resistance of the tissue of lowered by inflammation or injury [8].

More localization of the infiltrate around nerves, sweat glands and arrector pili gives evidence that leprosy bacilli can be transmitted through an ascending neuritis from nerve terminal of the skin. Liu et al believe that neurological invasion and extension is the important route of infection with *Myco. Leprae*.

Histopathological findings of tuberculoid (clinical) lesions

Epidermis: Hypertrophic changes associated with atrophy were found in 5 patients. Epithelial hyperplasia was noted in 1 patient and Spongiosis was noted in 1 case .

Dermis: Dermal infiltrate consisted of lymphocytes, epitheloid cells and giant cells with formation of typical tuberculoid granuloma in 5 patients. In the remaining 1 patient an epitheloid granuloma with scattered foci of

lymphocytes (histopathology of BB) was seen (16.67%) Grenz zone is noticed in this patient.

Skin Appendages: Arrector pili muscles: Inflammatory infiltrate consisting of lymphocytes and epitheloid cells was seen in all the 6 cases (100%).

Sweat Glands: Inflammatory changes were observed in all the 6 cases (100%). No other changes were seen.

Hair follicle and sebaceous glands: Inflammatory changes were seen in all the 6 cases (100%).

Nerves: All the 6 patients (100%) had perineural infiltration consisting of lymphocytes and epitheloid cells. The findings are in agreement with the characteristic histopathological features of tuberculoid leprosy described earlier.

Focal epithelial atrophy is a predominant feature in this group. No other significant changes were noted in epithelium. Appendages of the skin were showing inflammatory infiltrate in all the patients, four of these patients presented with total loss of sensation and all of them were tuberculoid leprosy histopathologically also. One 12 years old child presented with diminished loss of sensation over the lesion and histopathology of this lesion was different (revealed BB histopathologically.)

This patient might be undergoing downgrading reaction in the absence of treatment. Ridley (1971) maintains that during the process of upgrading or downgrading, there may occasionally be a confusing mixture of BT and BL.

Histopathological findings of borderline tuberculoid (clinical) lesions

Epidermis: Hypertrophy with areas of atrophy was present in 15 patients (55.55%), epithelial atrophy was present in 9 cases and epithelial hyperplasia was observed in 3 patients (11.11%). Spongiosis was seen in 3 cases (11.11%).

Dermis: The infiltrate of dermis consisted of predominantly lymphocytes and mononuclear cells. Macrophages were seen in few cases. There was no attempt at granuloma formation in majority of these cases. Grenz zone was absent in majority of these cases and increase amount of melanin was seen in many cases.

Skin Appendages: Arrector pili muscle atrophy was noted in 5 cases (18.5%). Inflammatory changes were seen in 15 cases (55.55%) while no changes were seen in 7 cases (25.92%). Sweat glands were not demonstrable in 2 cases (7.4%).

Hair Follicles and Sebaceous Glands: Inflammatory changes were seen in 19 patients (70.37%) while 6 cases (22.22%) did not show any changes. Hair follicle atrophy was seen in 2 cases (7.4%).

Nerves: There was perineural infiltration in 16 cases (59.25%) the infiltrate consisting of lymphocytes and mono nuclear cells while no changes in nerves were observed in 7 cases (25.92%). The nerves were not demonstrable in 4 cases (14.81%).

This group consisted of cases with variable histopathological findings. Majority of the cases were diagnosed histopathologically as nonspecific dermatitis. Another major section of the group is consistent with a histopathological diagnosis of indeterminate leprosy. One case revealed histopathological findings consistent with tuberculoid type.

Interesting in the present study are two patients manifesting histopathological features of borderline leprosy (BB). B.P Chattopadhyay et al (1990) reported a case which clinically presented as borderline tuberculoid leprosy but biopsy findings were in conformity with histopathological diagnosis of borderline leprosy (BL).

C.K Job et al. (1985) also have reported a case of single leprosy lesion manifesting histopathologically as lepromatous leprosy (Sub Polar) [9].

In the absence of the treatment these patients are probably downgrading towards the lepromatous spectrum of the disease (but the duration was less than 2 years in the above two cases).

Clinico Histopathological Correlation

A Pathological entity like leprosy needs an appropriate classification because of its varied clinical manifestations. The most recent and widely accepted classification is that of Ridley and Jopling. (1966) for research purpose which is primarily based on immunity but has been correlated with clinical, histopathological and bacteriological findings. [10]. Ridley (1972) further endeavoured to improve on this classification. [11, 12, 13]. Despite having such an accurate classification there

is so much dissociation between clinical and histopathological features.

In this present study, the histopathological findings were consistent with clinical diagnosis in 13 (32.5%) cases while Sehgal (1977) reported consistent histopathology in 33.7% cases. Sehgal et al (1990) in a study of 82 cases observed histopathological conformity in 35 (42.7%) of cases [14]. Sunil Gupta et al in a study of 93 cases have observed overall histopathological conformity in 9 cases (9.7%) only. V.T Jerath and Desai [15] (1982) have reported histopathological conformity in 68.5% of cases. Mayers et al (1979), however, in a large series of 1429 cases noticed complete agreement in clinical and histopathological diagnosis in 77.2% of cases [16].

All the above studies have included multiple leprosy lesions in addition to single leprosy lesions whereas in the present study exclusively single leprosy lesions were undertaken for study.

Khanolkar (1964) encountered the characteristic features of both lepromatous and tuberculoid type in the same section and in a series of sections from the same biopsy [17]. C.K Job et al have even reported histopathological picture of lepromatous leprosy in a single leprosy lesion. In the present study there is more histopathological conformity among tuberculoid lesions (82.13%) while widespread clinico histopathological variation (85.19%) was noted in borderline tuberculoid cases and indeterminate cases (42.86%). Thus clinico histopathological disparity was more in borderline forms (BT) than in polar forms (TT) in leprosy.

Conclusion

There is wide disparity in clinico histopathological correlation in single lesions in leprosy in the present study. This may be due to the disease changing its spectrum depending upon the immunity of the host. Further studies are required in this regard.

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