

Histopathological Study of Leprosy Patients in a Tertiary Care Hospital in Navi Mumbai

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ABSTRACT

Background: Leprosy or Hansen's disease is a chronic infectious disease that mainly affects skin and peripheral nerves. Histopathology and demonstration of lepra bacilli is a vital tool to supplement clinical examination and diagnosis for correct classification and therefore treatment of patients.

Aim: To study histopathology of leprosy cases and identify histological types in patients in a tertiary care hospital in Navi Mumbai.

Materials and Methods: 50 skin biopsies diagnosed as leprosy over a period of two years from January 2017 to December 2018 were studied. Haematoxylin-eosin and Fite-Faraco staining for demonstrating lepra bacilli were done.

Results: Male to female ratio of patients was 4.5:1. Maximum number of cases was seen in the 3rd decade of life. The commonest histological type was borderline tuberculoid (18 cases, 36%), followed by tuberculoid type (8 cases, 16%); least common cases were of borderline lepromatous, indeterminate and histoid types (4 cases, 8%). The most common site was forearm (26%). All 12/50(24%) patients with affected nerves showed ulnar nerve involvement. Hypopigmented, anaesthetic plaque was the commonest clinical feature followed by erythematous lesions. All cases of histoid and lepromatous type showed acid-fast bacilli on Fite stain. Tuberculoid cases showed perineural infiltration and well-formed granulomas, borderline tuberculoid type showed additional feature of giant cells and lepromatous types showed grenz zone and no granulomas. Histoid type showed fusiform histiocytes resembling spindle cells.

Conclusion: Histopathological examination is the gold standard for accurate diagnosis and typing of leprosy. It should be done in all leprosy cases presenting to the clinician.

Key words: leprosy, histomorphology, borderline tuberculoid, lepromatous, granuloma, skin biopsy

INTRODUCTION

Leprosy is one of the most ancient diseases known to mankind. It is a chronic, debilitating, granulomatous disease caused by *Mycobacterium leprae*. The bacteria were discovered by Hansen in 1837. Interestingly, the organism cannot be cultured.^[1] It is an important public health menace, being prevalent throughout many areas in India and still carrying a social stigma for the patients affected. Leprosy

mainly affects the skin, causing lesions and anaesthesia, along with enlarged and thickened peripheral nerves.^[2] It has different histopathological forms depending on the immunity of the patient.^[3] The Ridley-Jopling classification is the most widely used and divides the disease into tuberculoid (TT), borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL) and lepromatous leprosy (LL), based on clinical, immunological and

histomorphological factors. [4] Indeterminate forms include types that do not fit into any of the five categories. Histoid leprosy is an uncommon type of LL that shows nodules or plaques over apparently normal skin. [5] This article aims to study the various histological types of leprosy in a tertiary care hospital over a period of two years.

MATERIALS AND METHODS

This was a retrospective study carried out over a period of two years from January 2017 to December 2018 at a tertiary care hospital in Navi Mumbai. Cases diagnosed as leprosy on histopathological examination from the skin biopsies sent

from the Department of Dermatology were included. Routine haematoxylin-eosin stain and Fite-Faraco stains were used for diagnosis.

RESULTS

The study shows a marked male predominance in cases diagnosed as leprosy (41 cases, 82%) as compared to females (9 cases, 18%). The male to female ratio was 4.5:1. Maximum number of cases was seen in the age group of 21-30 years, followed by the 4th and 5th decades of life. Maximum individual number of female and male patients was between the ages of 21-30 years (table 1).

Table 1: Distribution of leprosy cases according to age group and gender

Age (years)	Number of cases (Total = 50)	Percentage of cases (%)	Male (Total = 41)	Female (Total = 9)
0 – 10	-	-	-	-
11 – 20	6	12	5	1
21 – 30	14	28	10	4
31 – 40	10	20	8	2
41 – 50	10	20	8	2
51 – 60	4	8	4	0
61 – 70	6	12	6	0

Among total 50 skin biopsies, on histopathological examination, the most common type seen was borderline tuberculoid (18 cases, 36%), followed by 8 cases (16%) of the tuberculoid type, 6 cases (12%) each of lepromatous type and erythema nodosum leprosum (ENL), and 4 cases (8%) each of borderline lepromatous, indeterminate (IL) and histoid types (Figure 1).

The most common site was determined to be the forearm (26%), followed by the upper back (18%), the hand (10%), elbow and shoulder (8% each). Other sites involved were the face, neck, trunk, foot and buttocks among others. Out of all 50 cases, 60% were paucibacillary whereas 40% were multibacillary.

Nerve involvement was seen in 12 out of 50 patients (24% cases). All of them showed ulnar nerve involvement. The second commonest nerve to be involved was the posterior tibial, seen in 3 of the 12 patients who also had ulnar nerve involvement. Anterior tibial and radial nerve involvement was seen in 1 case each. No case of pure neuritic leprosy was observed in this study.

The most common presentation on clinical examination was the presence of single or multiple well-defined hypopigmented plaques with loss of sensations. The other types of skin lesions found were erythematous lesions, hypopigmented nodules, macules and papules (table 2).

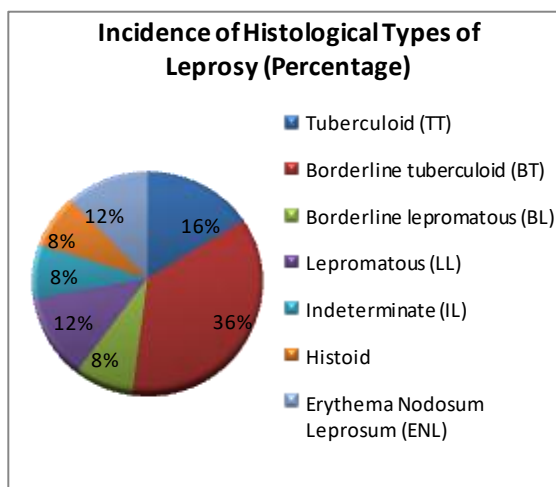


Figure 1: Percentage incidence of various histological types of leprosy

Table 2: Percentage of various types of skin lesions on clinical examination

Type of skin lesion	Percentage of cases (%)
Hypopigmented anaesthetic plaques	46
Erythematous lesions	28
Nodules	12
Macules	12
Papules	2

Fite-Faraco staining to identify acid-fast bacilli (AFB) was done in all 50 cases. It was positive in 25 (50%) of cases. No bacilli were noted in all cases of TT leprosy, whereas all cases of LL and Histoid types showed presence of acid-fast bacilli (table 3).

Table 3: Fite-Faraco positivity in individual histological type of leprosy

Histological type of leprosy (n=total number of cases of individual type)	Number of Fite-Faracopositivecases	Percentage of casesof individual type (%)
TT (n=8)	-	-
BT(n=18)	8	44
BL(n=4)	3	75
LL(n=6)	6	100
IL (n=4)	-	-
Histoid (n=4)	4	100
ENL (n=6)	4	66

On histopathological examination, epidermal and dermal changes were noted in the skin biopsies. Epidermal changes noted were presence or absence of atrophy, hyperplasia, hyperkeratosis, ulceration, orthokeratosis, spongiosis and acanthosis. Dermal changes noted were presence or absence of Grenz zone, perineural and perivascular inflammatory infiltrate, well-formed or ill-formed epithelioid cell granulomas, Langhans giant cells and foamy histiocytes. 25 (50%) cases showed epidermal atrophy, and 8 cases (16%) showed other epidermal changes like orthokeratosis/hyperkeratosis/spongiosis. 37 (74%) cases showed presence of granulomas in the dermis.

DISCUSSION

This was a retrospective study of 50 skin biopsies diagnosed as leprosy on histopathological examination in a tertiary care hospital in Navi Mumbai. Our study showed a marked male predominance with 4.5:1 being the male to female ratio. Similar findings have been observed in other studies as well. [1-4,6-11] Vasaikar et al have noted a slightly higher number of females in their study, with male to female ratio being 0.8:1. [12] The male majority has been attributed to more chance of contact in males due to occupation, and social inhibition and occupational factors regarding less reporting of cases in females in India. [1,8] The age of

the patients in this study ranged between 12 and 67 years. Most of the cases occurred in the 3rd decade, similar to other studies as well. [1, 2, 9-12] Kadam et al [7] found most of their cases to be between the ages of 35-55 years. Incidence in younger age group could be due to the endemic nature of leprosy. [3] As many of the lesions were present over exposed areas, this could also have led to noticing and reporting hence the concentration of cases in younger age group in this study.

Hypopigmented plaque with loss of sensation was the most common clinical feature observed (46%) which is comparable to other studies [3, 9-11] followed by erythematous lesions (28%). A hypopigmented patch over skin with loss of temperature sense and numbness is a characteristic feature seen in leprosy. Nerve involvement was seen with the ulnar nerve being typically involved, as was also seen in other studies. [1,7] One patient presented with claw hand deformity in our study, who was diagnosed on microscopy to have indeterminate leprosy. No trophic ulcers were seen in our study.

World Health Organization (WHO) in 1994 advocated the clinical categorization of leprosy cases into paucibacillary and multibacillary based on the number of lesions counted in a patient. [13] More than 5 lesions counted is said to be multibacillary; a count of less than or equal

to 5 lesions is typed as paucibacillary. According to this, 30 cases (60%) cases in our study were paucibacillary and 20 (40%) cases multibacillary. However, this method is unreliable as there may be miscounting and misreporting of cases. Thereby, histopathology is a crucial method of diagnosis.

The biopsies were classified according to the Ridley-Jopling classification on histopathological examination. Maximum numbers of cases in our study were of BT type; this is comparable to other studies. [1,4,7-12,14,15] Thapa et al [16] found the most common types to be both TT and BT (12 cases each) in their study. Khamankar et al [3] found LL to be the commonest histological type followed by BL. Pokhrel et al [17] found BT to be the least common (1 case) and TT to be the most common (14 cases) type. TT was the second commonest type in our study. Many patients exhibit a continuous shift over the immunological spectrum with progression and treatment of the disease. [1] This could be why a majority of patients were found to be of borderline type. With

treatment, they move towards the tuberculoid pole and without it they tend to shift towards lepromatous pole. [1] Patients with good immune status usually exhibit tuberculoid types and those with poor immunity usually tend to show lepromatous type lesions.

BT type (Figure 2A) typically shows nerve obliteration and erosion, with infiltration of neurovascular bundles, sweat gland and erector pili muscles by lymphocytes. Granulomas and Langhans giant cells are present. Few AFB may be demonstrated. TT type (Figure 2B) typically does not show giant cells and have well-formed epithelioid cell granulomas with nerve obliteration and rarely any AFB. [18] In our study, 8 out of 18 cases of BT were positive for Fite-Faraco. None of the TT cases showed any lepra bacilli. 55% of BT cases showed unremarkable epidermis and the remaining showed areas of atrophy and hypertrophy. In a study done by Ravindranath S., [6] 55.55% of BT cases showed variable areas of epidermal atrophy and hypertrophy.

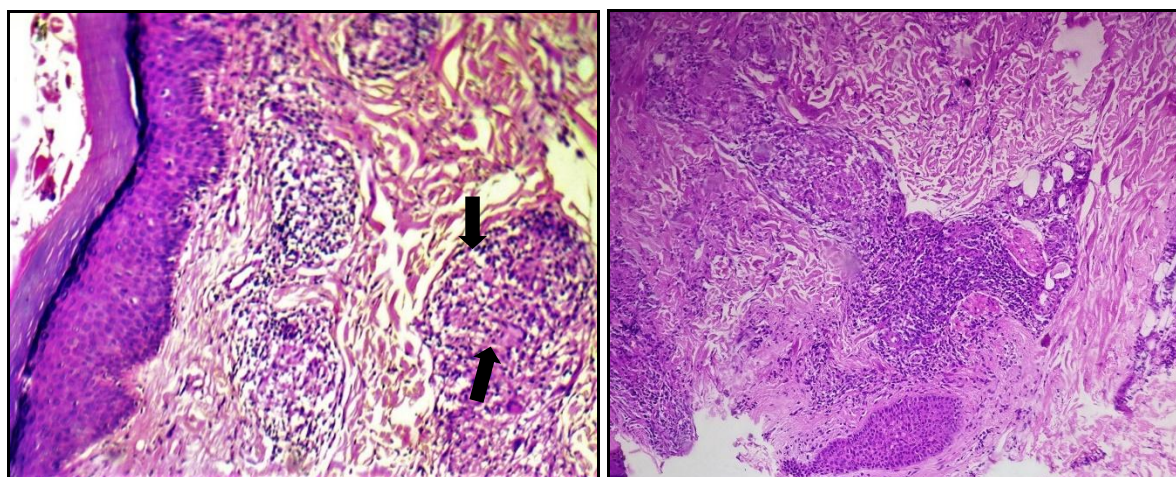


Figure 2A: BT leprosy showing epithelioid granulomas with few Langhans giant cells (black arrows).

Figure 2B: Dermis in TT leprosy shows heavy infiltration of nerve and hair follicle by lymphocytes and histiocytes.

BL type (Figure 3A) usually shows poorly formed granulomas. Foamy macrophages may not be conspicuous and globi (numerous bacilli clumped in macrophages) are usually not seen. LL type in our study showed the presence of a characteristic grenz zone (Figure 3B) which is a clear

space of normal collagen without any cellular infiltrate just beneath the flattened epidermis. Globi are often present and there is no attempt to form granulomas, though diffuse lymphoplasmacytic infiltration is present. [18] All LL cases and 75% BL cases showed AFB positivity (Figure 3C).

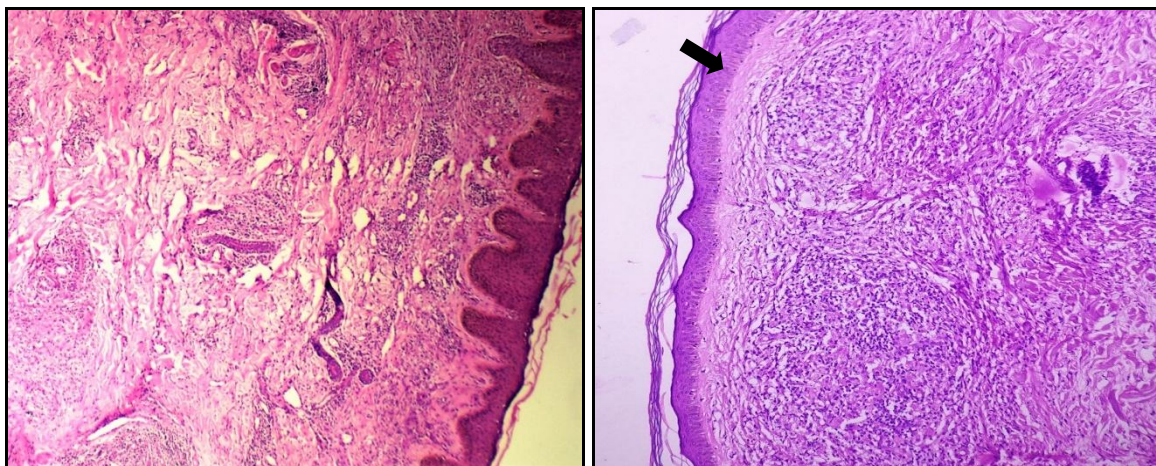


Figure 3A: BL type showing poorly formed granulomas. **Figure 3B:** LL type shows flattened epidermis with characteristic grenz zone (black arrow) and no granulomas but diffuse cellular inflammatory infiltrate and foamy macrophages.

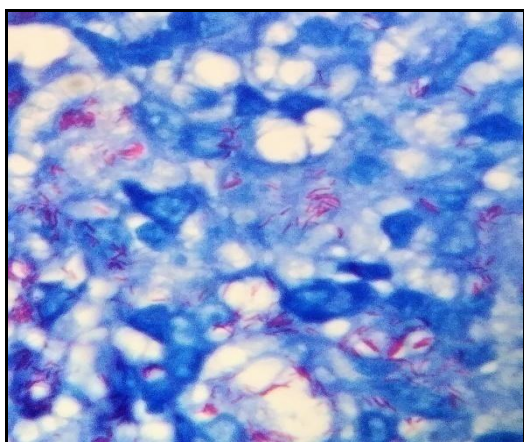


Figure 3C: Numerous acid-fast lepra bacilli seen in a case of LL leprosy (Fite-Faraco x100).

IL type represents those cases that have histopathological and clinical features of leprosy but do not fit into the Ridley-Jopling classification. This is an early, transitory lesion seen in patients with variable immunological status.^[15] It may be difficult to elicit anaesthesia on facial patches, especially in children. These cases

showed lymphocytic infiltration of the nerves and erector pili muscles, but no definite granulomas (Figure 4). In our study, a patient who presented with claw hand was diagnosed with IL. Only 1 out of 4 cases showed AFB positivity.

Histoid leprosy, coined by Wade in 1963, is an uncommon type of lepromatous leprosy showing spindle cells which are fusiform histiocytes arranged in storiform pattern that contain the AFB. There is no globus formation and a grenz zone is often seen. Patients on discontinuous dapsone therapy often show this type.^[5] These often show high number of AFB, almost resembling sheaves of wheat.^[18] Our 4 cases showed similar histopathological features and clinical history (Figure 5). Epidermal atrophy was seen; this has been explained by dermal expansion due to underlying fusiform cells.^[5,18]

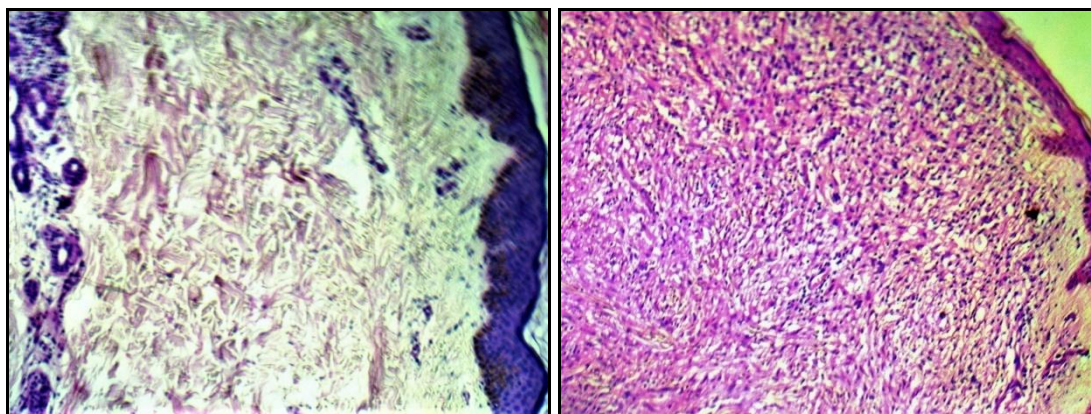


Figure 4: IL type showing no granulomas and lymphocytic infiltration around nerves and sweat glands. **Figure 5:** Histoid type showing flattened epidermis and spindle-like cells in the dermis in a storiform pattern.

Delayed hypersensitivity reactions in leprosy are divided into types 1 and 2. Type 2 reactions (ENL) show dermal abscess formation, with neutrophils and foamy macrophages and numerous bacilli. [18] Similar features were seen in the 6 cases in our study (Figure 6). These are associated with immune complex deposition and may be seen in untreated cases or LL patients on treatment. [1]

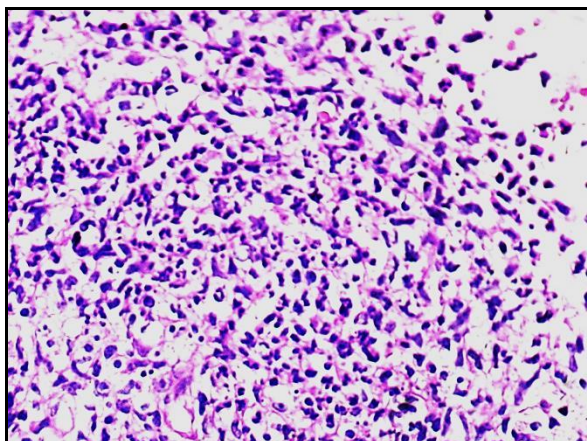


Figure 6: High power view of a case of ENL showing neutrophils and some debris in the dermis.

CONCLUSION

Histopathological examination of skin lesions is a crucial method and the gold standard for accurate diagnosis and typing of leprosy. [9] Combined with Fite staining, it is very important in cases where insufficient clinical history is available, in paediatric cases and in early/ borderline/ indeterminate/histoid cases which may not have characteristic clinical signs and show overlapping. It is also helpful in cases where patients may not have anaesthetic patches, especially on the face, and those with vague erythematous nodules or papules where leprosy is suspected. Biopsy is a minimally invasive and easy method as well. Thus, histopathology and demonstration of acid-fast lepra bacilli is recommended in all cases of leprosy for a good clinicopathological correlation and diagnostic accuracy, which would ultimately help in the prognosis and line of treatment of the patient.

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