Original article:

Significance of histopathology in accurate diagnosis of leprosy

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Abstract:

Context: Leprosy still continues to be an important public health problem. Leprosy is one of the leading causes of physical disabilities, which contribute to intense social stigma resulting in discrimination of patients and their families. Leprosy is a chronic infectious disease caused by Mycobacterium leprae, principally affecting the cooler parts of the body, mainly skin and peripheral nerves; it also involves muscles, eyes, bones, testis and internal organs.

Materials and Methods: Skin biopsies after adequate fixation in 10% of formalin, were routinely processed and paraffin embedded sections of 5 µ thickness were stained with H and E and fite-faraco stain and were studied microscopically.

Results & Conclusion: This study thus makes it mandatory to study tissue biopsy findings in all leprosy patients which were not considered relevant for treatment purposes until now, and thus could be given a status in the categorization and assessment of severity of the disease.

Key words: Histomorphology, leprosy

Introduction:

Leprosy is one of the leading causes of physical disabilities, which contribute to intense social stigma resulting in discrimination of patients and their families. Leprosy is a chronic infectious disease caused by Mycobacterium leprae, principally affecting the cooler parts of the body, mainly skin and peripheral nerves; it also involves muscles, eyes, bones, testis and internal organs.

Leprosy is known, since ancient times as “Kushtaroga.” The causative agent of leprosy, M. leprae, was discovered in 1873 by Armauer Hansen. [1] Even though, it was discovered early, it has not been cultured as yet.Leprosy is an important public health problem in most of the developing countries. Hence control of communicable disease is based on on identifying and destroying or attacking the causative organism. [2]

The clinical manifestations of leprosy are so varied and diverse and can mimic a variety of unrelated diseases. Presentation may vary from an insignificant skin lesion to extensive disease causing profound disability/deformities. Histopathological study of leprosy is very important in understanding the disease, its varied manifestation and complications. Hence clinicopathological correlation is extremely important in patient care and management.[2] The present study (prospective study) on histomorphological analysis of skin biopsies in leprosy was undertaken in Department of Pathology, J.J.M. Medical College.

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Materials and Methods:

Materials for the study consisted of skin biopsies obtained from patients clinically diagnosed with leprosy who attended either Out-patient Department of leprosy clinics of Chigateri District Hospital and Bapuji Hospitals that are attached to

J.J.M. Medical College, Davangere.

Skin biopsies were obtained by incisional biopsy performed by the Dermatologist and were sent to the Department of Pathology in 10% of formalin. After adequate fixation

for about 8-12 hours, the biopsies were submitted for routine processing, following which the paraffin embedded sections of 5 µ thickness were stained with Hematoxylin and Eosin (H and E) for morphological analysis and Wade Fite staining for identifying the bacilli. The procedure followed for Fite Faraco Stain was Wade-Fite method for M. leprae in paraffin section (modified from Klade, 1957). The procedure was slightly modified in the present study. The procedure followed for Fite Faraco Stain was Wade-Fite method for M. leprae in paraffin section.

Results:

TABLE 1: HISTOPATHOLOGY OF DERMISHistopathology of Dermis	**Types of Leprosy**					
	TT	**BT**	**BB**	**BL**	**LL**	**IL**
	2	57	7	17	16	1
Epithelioid Granuloma	2(100%)	4(7.01%)	0	0	0	0
Giant cells	2(100%)	17(29.82%)	3(42.85%)	2	0	0
Lymphocytes around						
Arrector Pilorum (AP)	0	27(47.36%)	3(42.85%)	7(41.17%)	10(62.5%)	0
Appendages(A)	0	17(29.82%)	1(14.28%)	10(58.82%)	11(68.75%)	1(100%)
NV Bundles(NV)	0	39(68.42%)	0	8(47.05%)	9(56.25%)	0
Lymphohistiocytic aggregates around						
Arrector Pilorum(AP)	2(100%)	34(59.64%)	6(85.71%)	0	0	0
Appendages (A)	1(50%)	27(47.36%)	6(85.71%)	0	0	1(100%)
NV Bundles(NV)	2(100%)	39(68.42%)	5(71.42%)	0	0	0
Macrophages in diffuse sheets around						
Arrector Pilorum(AP)	0	0	7(100%)	17(100%)	16(100%)	0
Appendages(A)	0	0	7(100%)	17(100%)	16(100%)	0
NV Bundles(NV)	0	0	7(100%)	17(100%)	16(100%)	0
Grenz Zone	0	0	1(14.28%)	8(47.05%)	11(6.25%)	0

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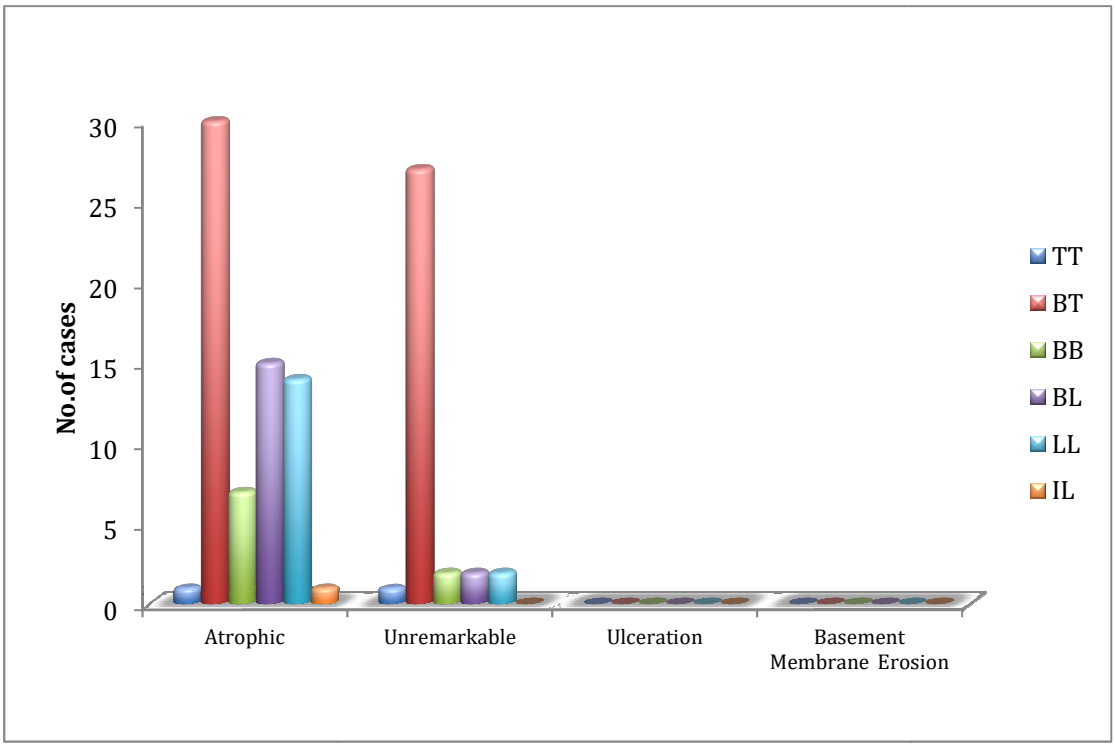
TABLE 2 : HISTOPATHOLOGY OF EPIDERMIS

Histopathology of Epidermis	Types of Leprosy						Total
	Types	TT	BT	BB	BL	LL	IL	
	No	2	57	7	17	16	1	100
Atrophic		1(50%)	30 (52.63%)	5 (71.42%)	15 (88.23%)	14 (87.5%)	1(100%)	66 (66%)
Unremarkable		1(50%)	27 (47.36%)	2 (28.57%)	2 (11.76%)	2 (12.5%)	0	34 (34%)
Ulceration		0	0	0	0	0	0	0
Basement Membrane Erosion		0	0	0	0	0	0	0



100 skin biopsies were studied for the various epidermal changes . In 66 (66%) the epidermis was atrophic, and in 34(34%) it was unremarkable .

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TABLE 3 : HISTOPATHOLOGY OF EPIDERMIS IN TT

Type	No	Atrophic	Unremarkable	Ulceration	BM Erosion
TT	2	1(50%)	1(50%)	0	0

Of the 2 biopsies in this category, epidermis was atrophic in 1 (50%) and unremarkable in 1 (50%).

TABLE 4 : HISTOPATHOLOGY OF EPIDERMIS IN BT

Type	No	Atrophic	Unremarkable	Ulceration	BM Erosion
BT	57	30(52.63%)	27(47.36%)	0	0

Of the 57 biopsies in this category , epidermis was atrophic in 30 (52.63%) and unremarkable in 27 (47.36%).

TABLE 5 : HISTOPATHOLOGY OF EPIDERMIS IN BB

Type	No	Atrophic	Unremarkable	Ulceration	BM Erosion
BB	7	5(71.42%)	2(28.57%)	0	0

Of the 7 biopsies in this category , epidermis was atrophic in 5(71.42%) and unremarkable in 2 (28.57%).

TABLE 6 : HISTOPATHOLOGY OF EPIDERMIS IN BL

Type	No	Atrophic	Unremarkable	Ulceration	BM Erosion
BL	17	15(88.23%)	2(11.76%)	0	0

Out of 17 biopsies in this category, epidermis was atrophic in 15(88.23%) and unremarkable in 2 (11.76%).

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TABLE 7 : HISTOPATHOLOGY OF EPIDERMIS IN LL

Type	No	Atrophic	Unremarkable	Ulceration	BM Erosion
LL	16	14(87.5%)	2(12.5%)	0	0

Out of the 16 biopsies in this category, epidermis was atrophic in 14(87.5%) and unremarkable in 2 (12.5%).

TABLE 8 : HISTOPATHOLOGY OF EPIDERMIS IN IL

Type	No	Atrophic	Unremarkable	Ulceration	BM Erosion
IL	1	1(100%)	0	0	0

Out of 1 biopsy in this category , epidermis was atrophic in 1 (100%).

TABLE 9 : HISTOPATHOLOGY OF DERMIS

Histopathology of Dermis	**Types of Leprosy**					
	TT	**BT**	**BB**	**BL**	**LL**	**IL**
	2	57	7	17	16	1
Epithelioid Granuloma	2(100%)	4(7.01%)	0	0	0	0
Giant cells	2(100%)	17(29.82%)	3(42.85%)	2	0	0
Lymphocytes around						
Arrector Pilorum (AP)	0	27(47.36%)	3(42.85%)	7(41.17%)	10(62.5%)	0
Appendages(A)	0	17(29.82%)	1(14.28%)	10(58.82%)	11(68.75%)	1(100%)
NV Bundles(NV)	0	39(68.42%)	0	8(47.05%)	9(56.25%)	0
Lymphohistiocytic aggregates around						
Arrector Pilorum(AP)	2(100%)	34(59.64%)	6(85.71%)	0	0	0
Appendages (A)	1(50%)	27(47.36%)	6(85.71%)	0	0	1(100%)
NV Bundles(NV)	2(100%)	39(68.42%)	5(71.42%)	0	0	0
Macrophages in diffuse sheets around						
Arrector Pilorum(AP)	0	0	7(100%)	17(100%)	16(100%)	0
Appendages(A)	0	0	7(100%)	17(100%)	16(100%)	0
NV Bundles(NV)	0	0	7(100%)	17(100%)	16(100%)	0
Grenz Zone	0	0	1(14.28%)	8(47.05%)	11(6.25%)	0

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TABLE 10: HISTOPATHOLOGY OF DERMIS IN TT

TT	Epithelioid granulomas	Giant cells	Lymphocytes around			Lymphohistocytes around			ges around	ges around	ges around	Grenz zone
			AP	A	NV	AP	A	NV				
2	2(100%)	2 (100 %)	0	0	0	2 (100 %)	1 (50%)	2 (100 %)	0	0	0	0

Of the 2 biopsies in this category, epithelioid granulomas were seen in 2 (100%), giant cells were seen in 2 (100%), lymphohistiocytic aggregates were present around arector pilorum in 2 (100%), around appendages in 1 (50%) and around neurovascular bundles in 2 (100%).

TABLE 11 : HISTOPATHOLOGY OF DERMIS IN BT

BT	Epithelioid granulomas	Giant cells	Lymphocytes around			Lymphohistocytes around			ges around	ges	ges around	Grenz zone
			AP	A	NV	AP	A	NV				
57	4 (7.01 %)	17 (29.82%)	27 (47.3 6%)	17 (29.8 2%)	39 (68.4 2%)	34 (59.6 4%)	27 (47.3 6%)	39 (68.4 2%)	0	0	0	0

Of the 57 biopsies in this category, epithelioid granulomas were seen in 4 (7.01%), and giant cells were seen in 17 (29.82%). Lymphocytes were present around arector pilorum in 27(47.36%), around appendages in 17(29.82%), and around neurovascular bundles in 39(68.42%). Lymphohistiocytic aggregates were present around arector pilorum in 34(59.64%), around appendages in 27 (47.36%) and around neurovascular bundles in 39 (68.42%).

TABLE 12 : HISTOPATHOLOGY OF DERMIS IN BB

BB	Epithelioid granulomas	Giant cells	Lymphocytes around			Lymphohistocytes around			Macrophages around AP	Macrophages Around A	Macrophages around, NV	Grenz zone
			AP	A	NV	AP	A	NV				
7	0	3 (42. 85%)	3 (42 .85 %)	1 (14 .28 %)	0	6 (85 .71 %)	6 (85 .71 %)	5 (71 .42 %)	7(100%)	7(100%)	7(100%)	1 (14.2 8%)

Of the 7 biopsies in this category , giant cells were seen in 3 (42.85%). Lymphocytes around arrector pilorum were seen in 3(42.85%) and around appendages in 1 (14.28%). Lymphohistiocytic aggregates were seen around arrector pilorum in 6(85.71%), around appendages in 6(85.71%) and

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around neurovascular bundles in 5 (71.42%). 7(100%) biopsies showed macrophages around arrector pilorum, appendages and neurovascular bundles . Grenz zone was present in 1 (14.28%) biopsy.

TABLE 13 : HISTOPATHOLOGY OF DERMIS IN BL

BL	Epithelioid granulomas	Giant Cells	Lymphocytes Around AP	Lymphocytes Around A	Lymphocytes around NV	Lymphohistiocytes around AP	Lymphohistiocytes around A	Lymphohistiocytic aggregates around NV	Macrophages around AP,	Macrophages around A	Macrophages around NV	Grenz zone
17	0	0	7(41.17%)	10(58.82%)	8(47.05%)	0	0	0	17(100%)	17(100%)	17(100%)	8 (47.05%)

Of the 17 biopsies in this category, lymphocytic infiltration around arrector pilorum was seen in 7 (41.17%), around appendages in 10(58.82%), and around neurovascular bundles in 8 (47.05%). All 17 biopsies showed macrophages around arrector pilorum, appendages and neurovascular bundles. Grenz zone was present in 8 (47.05%).

TABLE 14: HISTOPATHOLOGY OF DERMIS IN LL

LL	Epithelioid granulomas	Giant Cells	Lymphocytes around AP	Lymphocytes around A	Lymphocytes around NV	Lymphohistiocytes around AP	Lymphohistiocytes around A	Lymphohistiocytes around NV	Macrophages Around AP	Macrophages around A	Macrophages around NV	Grenz zone
16	0	0	10 (62.5%)	11 (68.75%)	9 (56.25%)	0	0	0	16(100%)	16(100%)	16(100%)	11 (68.75%)

Of the 16 biopsies in this category, lymphocytic infiltrate was seen around arrector pilorum in 10(62.5%), around appendages in 11(68.75%) and around neurovascular bundles in 9 (56.25%). 16 biopsies showed macrophages around arrector pilorum, appendages and neurovascular bundles. Grenz zone was seen in 11 (68.75%) biopsies.

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Discussion:

Leprosy patients with 1-5 skin lesions are grouped together as PB for treatment purposes. This study reveals that patients with 1-5 skin lesions present with varied clinical and histopathological features which points to the nonhomogeneous nature of this group. Two patients with clinical features of BT leprosy had BIG of 1+ on skin biopsy, which highlights the importance of Fite faraco stain on skin biopsies which reveals the presence of M. leprae bacilli better than SSS, thus indicating the importance of histopathology and AFB stain on skin biopsy to rule out MB type in patients clinically grouped as PB type. The significance of our observation is that patients with 1-5 skin lesions do not have disease of similar severity, and can reveal AFB in few of them. It is known that clinical features in leprosy patients reflect only the gross morphology of the underlying pathological changes. Significant discrepancies have been reported between the bacteriological and immunological status of the nerve and skin compared to the clinical diagnosis. [4],[5],[6] These features should also be considered while establishing treatment programs for leprosy. [7] It has been observed that a few BT patients harbor AFB in their nerves for many years, even though they become clinically inactive following MDT. [8] Explanation for this could lie in defective macrophage function. Bacterial clearing capacity within a lepromin-induced granuloma is not invariably present in all tuberculoid and indeterminate leprosy patients. [9]

Conclusion:

This study thus makes it mandatory to study tissue biopsy findings in all leprosy patients which were not considered relevant for treatment purposes until now, and thus could be given a status in the categorization and assessment of severity of the disease.

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