Original article

# Histological changes in the epidermis of normal appearing skin in leprosy

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## Abstract

**Introduction**: The micro pathological changes in epidermis, nerves and skin appendages from skin lesion in leprosy are common but reports of involvement of apparently normal sites are few. During the latent period the apparently normal skin might also be undergoing some pathological changes. The objective of this study is to observe micro pathological changes in epidermis of apparently normal skin. Material and methods: We investigated skin biopsy material taken from 250 patients with clinically diagnosed leprosy. Biopsies were taken at least 10 cm away from site of lesion. Hematoxylin and eosin staining used to see histological changes in epidermis and Harada's modified allochrome method used to demonstrate acid-fast bacillus. Z test of proportion was used to evaluate significant difference between different histological features. **Results:** The pattern of leprosy among the patients were indeterminate in 65 cases (26.0%), tuberculoid in 45 cases (18.0%), borderline tuberculoid in 38 cases (15.2%), borderline leprosy in 36 cases (14.4%), borderline lepromatous in 34 cases (13.6%) and leopromatous leprosy in 32 cases (12.8%). The epidermis of normal appearing skin showed flattening and thinning, erosion and presence of AFB. **Conclusion**: Micropathological changes were seen in epidermis of normal appearing skin in all forms of leprosy but involvement was greater at the lepromatous end of the spectrum compared to tuberculoid end. Significant difference observed between two variables and presence of AFB is also significant as far as dissemination and transmission of disease is concerned.

**Keywords:** leprosy, epidermis, acid fast bacillus.

## 1 Introduction

Skin and peripheral nerves are the primary sites for leprosy caused by Mycobacterium Lepra (KOTTEESWARAN, CHAIKO and JOB, 1980; JOB, 1965; RIDLEY, 1984). India alone contributes to more than 1/3 rd cases of leprosy to the world. There are different pathological forms of leprosy depending on the immune status of the host (JOB, 1965). In subclinical stage the apparently normal looking skin might also be undergoing some pathological changes, therefore a reliable diagnosis hinges around a good histopathological diagnosis and demonstration of bacilli in histopathological sections (PANDAY and TAILOR, 2008; LUCUS and RIDLEY, 1989; NAYAK, SHIVARUDRAPPA, NAGARAJAPA et al., 2003).

## 2 Material and methods

250 patients with characteristic skin lesions of leprosy attending skin outpatient department were investigated. Patients with characteristic skin lesions, with or without systemic symptoms having no history of previous treatment and associated diseases like HIV/AIDS, Tuberculosis, Lymphoma, Leukemia etc were included in the study. Incision biopsies of all such patients (after obtaining their written consent) were taken at least 10 cm away from site of lesion. The biopsy was fixed in 10% formalin and processed for paraffin sectioning.

The following staining methods were applied for histological investigations:

- Hematoxylin and Eosin for histological changes; and
- Harada's modified Allochrome method for acid- fast bacilli (HARADA, 1977).

Work is approved by Ethics Committee of the institute.

## 3 Results

A total of 250 patients were included in this study. Histopathological findings were graded into tuberculoid (TT), borderline tuberculoid (BT), borderline leprosy (BB), borderline lepromatous (BL) and lepromatous leprosy (LL) according to Ridley and Jopling scale (1966). Sections showing scattered nonspecific lympho-histiocytic infiltration were classified as indeterminate leprosy (JOPLING and McDOUGALL, 1996). The pattern of leprosy among the patients were indeterminate (INDT) in 65 cases (26.0%), tuberculoid (TT) in 45 cases (18.0%), borderline tuberculoid (BT) in 38 cases (15.2%), borderline leprosy (BB) in 36 cases (14.4%), borderline lepromatous (BL) in 34 cases (13.6%) and leopromatous leprosy (LL) in 32 cases (12.8%).The micropathological changes were seen in epidermis in apparently normal site in all type of leprosy. Results presented in form of scatter diagram (Figure 1) and in Table 1. Micropathological changes include erosion of epidermis (Figure 2), thinning and

flattening of epidermis (Figure 3) and presence of acid-fast bacilli (Figure 4) in the epidermal cells.

Z test for proportion (double sample) was used to test the significant difference between different histological features i.e. thinning and erosion (Table 2), thinning and presence of A.F.B (Table 3), erosion and presence of AFB (Table 4).

## 4 Discussion

Reports on histological studies of uninvolved site in leprosy are few. In these studies either normal skin studied was very close to the lesion or the numbers of cases were less (GANAPATI, DESIKEN and IYER, 1972; REA, GOTTLIB and LEVAN, 1975; JOSE, JWAN and ROSA, 1981; TUTAKNE, DAS, AGGARWAL et al., 1983; VERMA, TUTAKNE and SHARMA, 1984).The present study differs from the other studies as 250 patients investigated and biopsy of apparently normal skin taken at least 10 cm away from lesion.

**Table 1.** Histological features of epidermis of apparently normal skin.

| Leprosy Spectrum | H &E Staining | | Harada allochrome staining |
|---|---|---|---|
| | Thinning | Erosion | AFB |
| Lepromatous Leprosy (LL-32) | 16 | 03 | 07 |
| Borderline Lepromatous (BL-34) | 13 | 03 | 06 |
| Borderline leprosy (BB-36) | 11 | 02 | 04 |
| Borderline Tuberculoid (BT-38) | 09 | 18 | 02 |
| Tuberculoid (TT-45) | 07 | 17 | 01 |
| Indeterminate (INDT-65) | 07 | 15 | 01 |

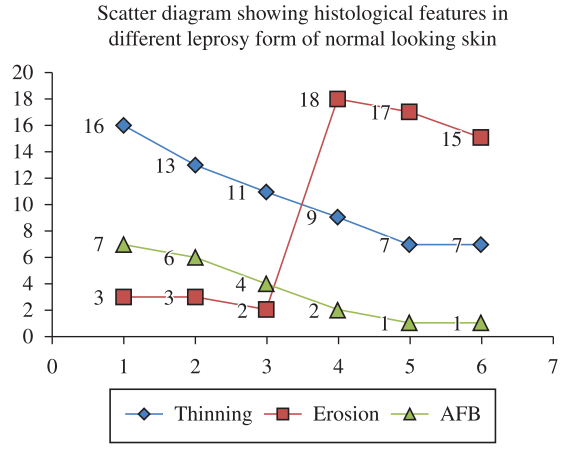


Figure 1. Vertical Axis- representing number of cases of thinning, erosion and AFB in different type of leprosy. Horizontal Axis- representing different types of leprosy. 1-Lepromatous 2-Borderline Lepromatous 3-Borderline Leprosy 4- Borderline Tuberculoid 5- Tuberculoid 6- Indeterminate.

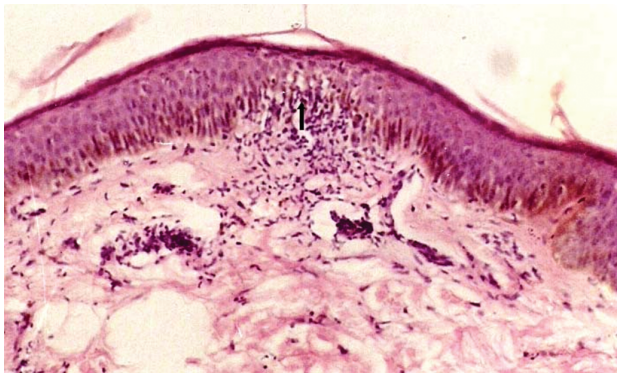


**Figure 2.** Photomicrograph showing the minimal sub epidermal infiltration with erosion of epidermis in the apparently normal skin of a TT case. Arrow indicates erosion. H&E 100×.

**Table 2.** Difference between thinning and erosion in various leprosy forms.

| Leprosy forms | Thinning | Erosion | Z-value | P-value | Significant/non significant |
|---|---|---|---|---|---|
| LL (32) | 16 | 03 | 3.28 | .001 < .05 | Significant |
| BL (34) | 13 | 03 | 2.57 | .010 < .05 | Significant |
| BB (36) | 11 | 02 | 2.45 | .014 < .05 | Significant |
| BT (38) | 09 | 18 | 1.92 | .055 > .05 | Non Significant |
| TT (45) | 07 | 17 | 2.14 | .032 < .05 | Significant |
| INDT (65) | 07 | 15 | 1.63 | .102 > .05 | Non Significant |

**Table 3.** Difference between thinning and AFB in various leprosy forms.

| Leprosy forms | Thinning | AFB | Z-value | P-value | Significant/non significant |
|---|---|---|---|---|---|
| LL (32) | 16 | 07 | 2.08 | .037 < .05 | Significant |
| BL (34) | 13 | 06 | 1.62 | .010 < .05 | Significant |
| BB (36) | 11 | 04 | 1.74 | .082 > .05 | Non Significant |
| BT (38) | 09 | 02 | 1.95 | .050 = .05 | Significant |
| TT (45) | 07 | 01 | 1.85 | .064 > .05 | Non Significant |
| INDT (65) | 07 | 01 | 1.85 | .064 < .05 | Non Significant |

**Table 4.** Difference between Erosion and AFB in various leprosy forms.

| Leprosy forms | Erosion | AFB | Z-value | P-value | Significant/non significant |
|---|---|---|---|---|---|
| LL (32) | 03 | 07 | 1.03 | .302 > .05 | Non Significant |
| BL (34) | 03 | 06 | 0.71 | .474 > .05 | Non Significant |
| BB (36) | 02 | 04 | 0.42 | .67 < .05 | Non Significant |
| BT (38) | 18 | 02 | 3.90 | .001 < .05 | Significant |
| TT (45) | 17 | 01 | 3.95 | .001 < .05 | Significant |
| INDT (65) | 15 | 01 | 3.47 | .000 < .05 | Significant |

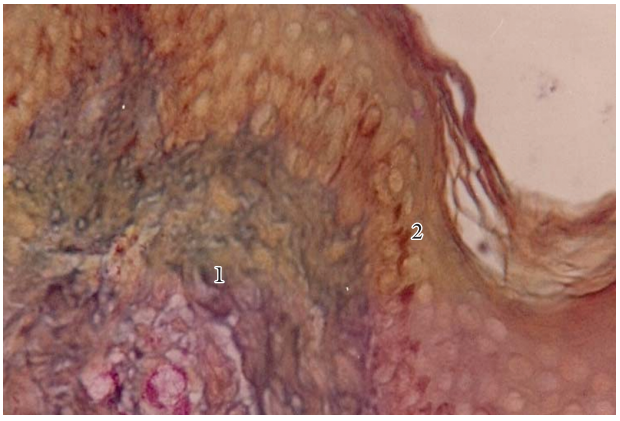


**Figure 3.** Photomicrograph showing granuloma in sub epidermal zone compressing overlying epithelium in the apparently normal skin of an indeterminate leprosy. 1. Sub epidermal granuloma 2. Thinned out epithelium. Modified Harada's allochrome method 400×.

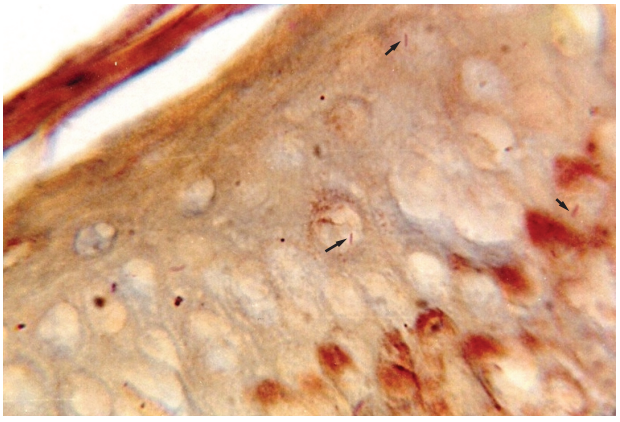

**Figure 4.** Photomicrograph showing the bacilli in the epidermal cells in different layer in the apparentaly normal skin of a LL case. Arrow indicates bacilli. Modified Harada's allochrome method 1000×.

Erosion of epidermis is a well known feature of tuberculoid leprosy (GANAPATI, DESIKEN and IYER, 1972; KHANOLKAR, 1955). In present study erosion was seen in 58 cases (15 INDT, 17 TT, 18 BT, 2 BB, 3 BL and 3 LL) of apparently normal skin. Erosion of epidermis in the indeterminate lesions indicates that it must be the one of the earliest manifestations of leprosy lesions which might develop into tuberculoid leprosy. However Ridley in 1971 and 1973 reported that the erosion of epidermis and other intra-epidermal lesions like focal infiltration of lymphocytes are the evidence of arresting the bacilli entering through the epidermis.

Presence of M. Leprae in epidermal cells is not reported more often because they are not ordinarily looked for in routine work. However electron microscopic studies (YOUNG, WOOK, HAE-YONG et al., 1955; OKADA, KOMURA and NISHIURA, 1978) revealed M. Leprae in the epidermal cells. In the present study we observed acid fast bacilli in epidermal cell of apparently normal skin of all forms of leprosy but presence of AFB was significantly low in INDT and TT forms as compared to LL and BL forms. Erosion was also less in cases where the AFB was visualized and there was significant difference between these two variables. Phagocytic nature of epidermal cells is a well known fact (OKADA, KOMURA and NISHIURA, 1978; MOTTAZ and ZELICKSON, 1967; KLAWS, 1969; CRUICKSHANK, COOPER and HOOPER, 1960). Bacilli close to basal layer of epidermis might have been phagocytosed by epidermal cells. Keratinocytes usually engulf bacilli from subepidermal zone; hence possibility of discharge of bacilli from intact skin should be seriously considered (JOB, JAYAKUMAR and ASCHHOFFS, 1999), on the other hand removal of keratin layer might result M. Leprae entering through intact epidermis (JOB, CHEHL, McCORMICK et al., 1985; LEIKER, 1977). Presence of bacilli in the epidermal cells becomes significant as far as dissemination and transmission of disease is concerned.

Ridley (1984) thought that flattening of epidermis is due to the pressure effect of expanding sub epidermal granuloma. In present study flattening of epidermis was seen in all forms of leprosy. however the percentage declines as we move from lepromatous to tuberculoid form, here the sub epidermal granuloma was large enough to compress overlying epidermis.

## 5 Conclusion

Micropathological changes were observed in epidermis of apparently normal skin of all types of leprosy. However involvement was more towards lepromatous end of spectrum. Bacilli were seen in prickle cell layer as well as surface keratin. The presence of M. Leprae in the epidermal cells proves beyond any reasonable doubt that M. Leprae are shed in large numbers even through intact skin, and therefore transmission of leprosy through skin and from skin to skin contact should be seriously considered.

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