

## Original Research Article

# Clinical and histopathological study of lepra reactions from a tertiary care center in South India

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## ABSTRACT

**Background:** Clinical features and histopathology of leprosy and type 1 and type 2 reactions do not always match, though they are generally accepted as important for arriving at a diagnosis. We studied the varied clinical presentations and the correlation with histology in patients presenting with leprosy and type 1 and type 2 reactions.

**Methods:** All patients with clinical features of leprosy and those with features of type 1 and type 2 lepra reactions attending the department of Dermatology from August 2008 to August 2009 were included. Detailed history, clinical examination and skin biopsy findings were noted and correlated using descriptive statistics.

**Results:** Of the 138 patients included in the study, 24 cases of reactions were detected. Eighteen had type 1 (75%) and six had type 2 (25%) reaction. Correlation showed that dermal edema on histology was helpful in diagnosis of lepra reactions while neutrophilic infiltration favoured the diagnosis of type 2 reactions.

**Conclusions:** Histopathological features are helpful in the diagnosis of lepra reactions, however in cases of doubt, the diagnosis should be made on clinical grounds.

**Keywords:** Type 1 lepra reaction, Type 2 lepra reaction

## INTRODUCTION

Leprosy is the best example of a disease showing an immunopathologic spectrum where by host immune reaction to the infective agent ranges from apparently none to marked, with a consequent range of clinicopathologic manifestations. The Ministry of Health Government of India has declared elimination of leprosy on 30th January 2006, but still cases continue to present to our department. Clinical features and histopathology of leprosy and type 1 and type 2 reactions do not always match, though they are generally accepted as important for arriving at a diagnosis.<sup>1-4</sup> Hence, we studied the varied clinical presentations and the correlation with histology in patients presenting with leprosy and type 1 and type 2 reactions.

## METHODS

All patients with clinical features of leprosy and those with features of type 1 and type 2 lepra reactions attending the Department of Dermatology from August 2008 to August 2009 were included, after obtaining informed consent. Patients not willing for biopsy were excluded.

A detailed history with special emphasis on type of lesions, sensory and motor symptoms and symptoms of lepra reactions was recorded in a predefined proforma. General and dermatological examination findings were noted. Complete hemogram, urinalysis, blood glucose, liver function tests and renal function tests were done in all patients. Ear lobe smears and slit skin smears from

representative skin lesions and normal skin were done and bacteriological and morphological indices were recorded.

Skin biopsy was done using a scalpel blade. Biopsy included the full depth of the dermis together with a portion of subcutaneous fat.

In case of pure neuritic leprosy nerve biopsy was done. A thickened cutaneous sensory nerve such as radial cutaneous nerve at wrist or sural nerve was chosen.

The biopsy specimen was stained with hematoxylin and eosin along with Fite-Faraco stain to demonstrate acid fast bacilli.

These clinical and histopathological findings were recorded and correlation between them was analysed using descriptive statistics.

## RESULTS

A total of 151 leprosy patients attended the department during the period, of which 13 patients not willing for biopsy were excluded. Twenty four (24) of the 138 patients developed lepra reactions. Eighteen had type 1 (75%) and six had type 2 (25%).

### Type 1 reaction

Majority of patients who developed type 1 reaction were of age group 20-40 years, with age ranging from 12 years to 85 years. Male: Female ratio was 2.6:1. Age distribution of patients with type 1 lepra reaction are shown in Table 1.

**Table 1: Age distribution of patients with type 1 lepra reaction.**

Age	Type 1 reaction	Percentage (%)
<20 years	3	16.7
20-40 years	8	44.4
40-60 years	5	27.8
>60 years	2	11.1

### Precipitating factors

Unknown in majority, administration of MDT was most common when identified (Table 2).

**Table 2: Precipitating factors for type 1 lepra reaction.**

Factor	No	Percentage (%)
MDT	7	38.9
Infection	2	11.1
Alcohol	1	5.6
Unknown	8	44.4

### Time of onset of reaction

Reaction was detected at time of diagnosis in 10 patients, within 6 months of starting MDT in seven patients and after 1 year of stopping treatment in one patient.

### Spectrum

Majority of patients developing type 1 reaction were from BT spectrum (72%) (Figure 1), but the probability of developing reaction was highest among BL and BB (42.8% and 100% respectively). HD at least risk of developing reaction was LL in this study (7.1%) (Table 3).



**Figure 1: Hansen's disease (borderline tuberculoid) with type 1 reaction.**

**Table 3: Clinical spectrum of HD developing type 1 reaction.**

Clinical spectrum	No of cases	No developing reaction	Percentage (%)
BT	8	13	72.2
BB	1	1	5.6
BL	7	3	16.7
LL	14	1	5.6
Pure neuritic	10	1	5.6

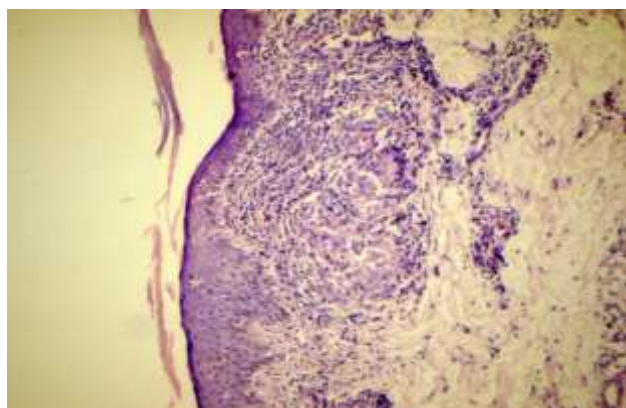
**Table 4: Clinical presentation of type 1 reaction.**

Clinical feature	Number	Percentage (%)
Skin lesion alone	7	38.9
Skin lesion + neuritis	8	44.4
Neuritis alone	3	16.7

Clinical presentation of type 1 reaction is summarized in Table 4.

Histopathological findings of type 1 reaction are given in Table 5. In 66.7% of patients (n=12) the histopathology was suggestive of same clinical spectrum of HD. Dermal

edema was observed in 61.1% (n=11) patients. Histopathology suggestive of higher spectrum of HD was noted in 33.3% (n=6) (Figure 2).



**Figure 2: Histopathology of type 1 reaction– dermal edema, granuloma and lymphocytes.**

**Table 5: Histopathology of type 1 reaction.**

Changes	No	Percentage (%)
Suggestive of same clinical spectrum of HD with dermal edema	9	50
Suggestive of same clinical spectrum of HD without dermal edema	3	16.7
Suggestive of higher spectrum of HD with edema	2	11.1
Suggestive of higher spectrum of HD without edema	4	22.2

### Type 2 reaction

There were six cases of type 2 reaction, age 22- 40 years, male: female ratio 2: 1.

MDT was the most common precipitating factor. Precipitating factors of type 2 reaction are summarized in Table 6.

**Table 6: Factors precipitating type 2 reaction.**

Precipitating factors	No	Percentage (%)
MDT	4	66.7
Infection	1	16.7
Unknown	1	16.7

### Onset

Two patients had type 2 reaction as initial presentation of HD. Four patients developed type 2 reaction within 6 months of starting MDT.

### Clinical spectrum

Constitutional symptoms were present in all cases of type 2 reaction. All patients had erythema nodosum leprosum (ENL) lesions. Erythema necroticans was present in two patients, of which one expired. There was pustular type of lesion in one patient. All patients had systemic features like fever and myalgia (Table 7).

**Table 7: Clinical spectrum of type 2 reaction.**

Presentation	No	Percentage (%)
Skin lesions alone	4	66.7
Skin lesions+neuritis	2	33.3

### Histopathology

83.3% (n=5) of cases showed dermal edema. Histological features of vasculitis were present in one patient with erythema necroticans (Table 8).

**Table 8: Histopathology of type 2 reaction.**

Changes	No	Percentage (%)
Underlying HD features only	1	16.7
Neutrophilic infiltration with dermal edema	4	66.7
Neutrophilic vasculitis with dermal edema	1	16.7

### Correlation

Dermal edema was found to be helpful in diagnosis both type 1 and type 2 lepra reactions on histology.

Neutrophilic infiltration favoured the diagnosis of type 2 reactions, being present in four out of six patients (66.7%).

## DISCUSSION

Of the 138 patients studied, eighteen patients developed type 1 and six patients developed type 2 lepra reactions.

### Type 1 reaction

Percentage of HD cases by spectrum developing type 1 reaction are compared with other studies from literature in table 8. BB patients are at maximum risk of developing type 1 reactions which is similar to the study by Brakel et al.<sup>5</sup> In our study one patient of the 10 patients with pure neuritic leprosy developed type 1 reaction. None of the other studies have patients with pure neuritic leprosy developing type 1 reaction. The histopathology in this patient were consistent with borderline tuberculoid.

Percentage of HD cases by spectrum developing type 1 reaction in comparison to other studies is given in Table 9.

**Table 9: Percentage of HD cases by spectrum developing type 1 reaction in comparison to other studies.**

Name of study	BT	BB	BL	LL	Pure neuritic
<b>Present study</b>	19	100	42.9	7.1	0.1
<b>Ramu et al<sup>6</sup></b>	35.6	48.9	15.6		
<b>Becx-Bleumink et al<sup>7</sup></b>	21		44	19	
<b>Van Brakel et al<sup>5</sup></b>	39	75	38	6.5	
<b>Scollard et al<sup>8</sup></b>	13	31	41		

In this study 38.9% of patient developed reaction for the first time during treatment. All those who developed reaction for the first time after MDT had it within 6 months after starting MDT. The same results were observed in similar studies.<sup>7,3,9</sup>

In patients with type 1 reaction, dermal edema on histopathology was present in 61.1% and histopathology was suggestive of same spectrum in 66.7%. In 33.3% of these patients, histopathological features were of higher spectrum indicating a reversal reaction. Moorthy et al showed histological features of same clinical spectrum in 55.6% cases and higher spectrum in 33.3%.<sup>4</sup>

### Type 2 reaction

Patients who developed type 2 reaction were in the age group 22-40, with maximum in between 30-40 years. Similar predominance of reaction in this age group were observed in some studies.<sup>10,11</sup> Percentage of BL and LL cases developing type 2 reaction in comparison to other studies are summarized in Table 10.

**Table 10: Percentage of BL and LL cases developing type 2 reaction in comparison to other studies.**

Study	BL	LL
<b>Present</b>	0	42
<b>Becx-Bleumink et al<sup>7</sup></b>	2.7	11
<b>Van Brakel et al<sup>5</sup></b>	1.9	32
<b>Scollard et al<sup>8</sup></b>	23	54
<b>Schreuder et al<sup>9</sup></b>	3.6	26

Factors precipitating type 2 reactions were MDT and infection. One patient had recurrent attacks of ENL with each monthly pulse of MDT. A similar observation was made by Brakel et al.<sup>5</sup>

Initial presentation of HD with type 2 reaction was seen in 33.3% of patients. Rea et al in their study reported that in 68.8% of patients with type 2 reaction it was the initial presentation of HD.<sup>12</sup>

Neuritis and nerve palsy were seen more frequently in type 2 reaction compared to type 1 reaction which was similar to the findings in a study by Brakel et al.<sup>5</sup>

Majority of cases with type 2 reaction showed neutrophilic infiltration in the background of foamy

macrophages as in previous studies. Dermal edema was present in most cases, again a feature described in earlier studies.

### CONCLUSION

The histopathology of both type 1 and type 2 reactions may aid in diagnosis, but the final diagnosis of reaction is made on clinical grounds. Histopathology should be carried out for definite diagnosis of leprosy and as an aid for classification of disease.

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