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Original Article

Type I Reaction in Leprosy - A Histopathological Analysis

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Even though type 1 lepra reaction (TIR) is a commonly encountered clinical problem, its histology has not yet been clearly delineated. This study attempts to enumerate the most sensitive parameters for the histological diagnosis of TIR. Case records between March 2007 and September 2007 of patients with TIR were reviewed and the biopsies were evaluated by a pathologist blinded to the previous diagnoses. Twenty three patients were included in the study. The most sensitive parameters in our study were dermal edema, intra-granuloma edema and giant cell size. Though clinical findings should remain the mainstay of diagnosis of TIR, the above mentioned parameters should be evaluated in biopsies of leprosy to look for signs of reaction which might otherwise be missed.

Key words : Hypersensitivity reaction, Borderline leprosy, intra-granuloma edema, dermatopathology

Introduction

Type I lepra reaction (TIR) is a delayed hypersensitivity reaction which is a major inflammatory complication of leprosy characterized by inflammation of skin lesions, nerves or both (Job 2001). TIR predominantly affects borderline states of leprosy. Skin lesions become erythematous, edematous and may ulcerate. Edema of the hands, feet and face may also be present though systemic symptoms are unusual (Ranque 2007). The diagnosis is usually made clinically. A skin biopsy is sometimes used to support the diagnosis. Interestingly, even experienced pathologists may under-diagnose reaction in skin sections from patients with clinically apparent TIR. Important diagnostic features appear to be intra-granuloma edema, dermal oedema, the presence of plasma cells and granuloma fraction. Standardized criteria for the diagnosis of TIR on histopathology are yet to be defined (Walker and Lockwood 2008).

A study by Lockwood et al (2008) has suggested that dermal and intra-granuloma edema, number and size of giant cells and HLA-DR expression are the most useful histological pointers to TIR. This study attempts to evaluate the usefulness of the histological parameters identified by Lockwood et al (2008).

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Methods

Case records of patients who presented to the hospital between March 2007 and September 2007 with a clinical diagnosis of TIR and underwent a skin biopsy prior to initiation of therapy were reviewed.

Twenty three patients with TIR were identified. The following clinical information was recorded: age, gender, Ridley Jopling classification, duration of symptoms of leprosy, duration of symptoms of TIR, previous treatment regimens and history of any reactional episodes in the past.

An expert pathologist who was blinded to the previous histopathological diagnosis reviewed the biopsies and classified them based on histopathological findings into the following categories.

1. Definite TIR
2. Probable TIR
3. Possible TIR
4. No evidence of TIR

The parameters mentioned by Lockwood et al (2008) were evaluated in all the cases. In addition, we also evaluated the composition of the granulomas and the vascular changes. The data was analyzed using Fischer's exact test and the P value for each of these parameters was calculated.

Results

Histopathologically, TIR was found to be present in 7(30.4%), probable in 4(17.39%), possible in 2(8.6%) and absent in 10(43.4%). The patients were divided into two groups based on this histopathological diagnosis, Group 1 consisting of cases diagnosed with definite and probable TIR and Group 2 consisting of cases with possible and no evidence of TIR.

Of the twenty-three patients, sixteen (69.6%) were clinically diagnosed as BT, one (4.3%) as BB and six (26%) as BL. In Group 1 the patients were almost equally divided among BT and BL spectrum whereas in Group 2 most patients 10 (91%) were in the BT spectrum. Smear positivity was seen in 5 of 11 cases in Group 1 but only in 2 of

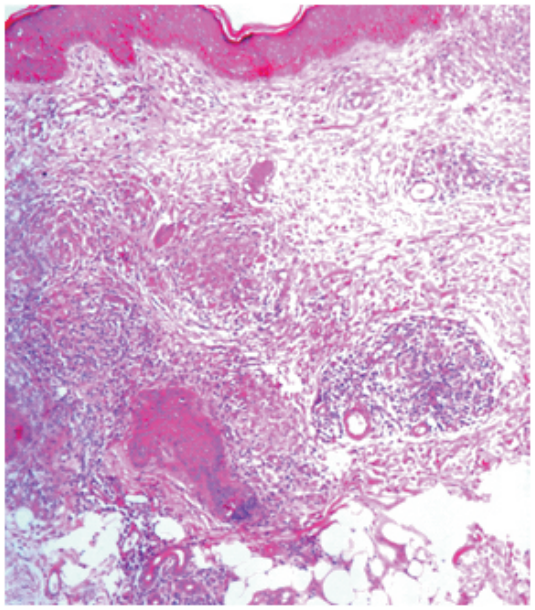

Fig 1 : Intra-granuloma and Peri-granuloma Edema with Large Giant Cells in Type I Reaction (H&E 10x)

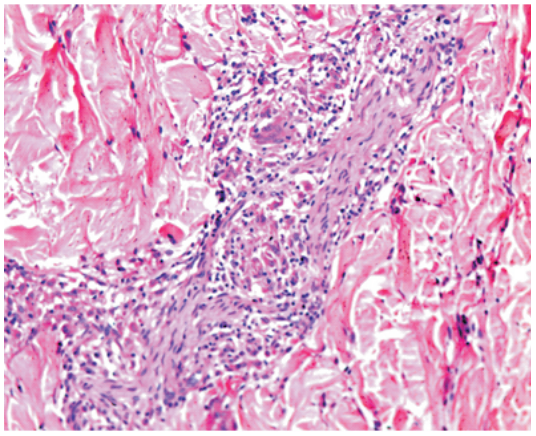

Fig 2 : Intra-neural Granuloma with Intra-granuloma Edema (H&E 40x)

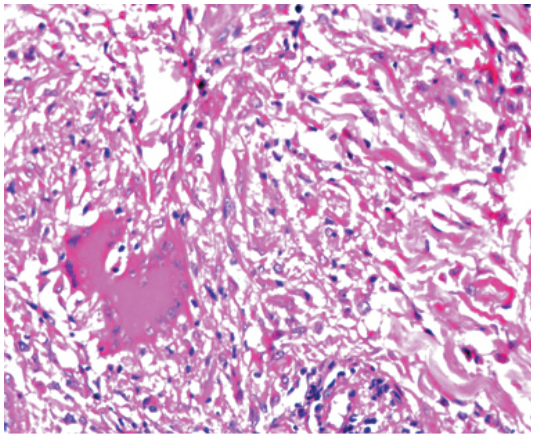

Fig 3 : Large giant cell (H&E 40x)

12 cases in Group 2. The significance of this finding is not clear.

All patients in Group 1 had flattening of the epidermal rete ridges. Nine (81.4%) cases in Group 1 had dermal edema which was prominent in the sub-epidermal zone as compared to 33.3% in Group 2. Loose granulomas with intra-granuloma edema were seen in all the patients in Group 1 and were absent in Group 2.

Most of the patients in Group 1 had medium to large foreign body giant cells which were irregular in shape (10, 90.9%). The giant cells and epithelioid cells within the granuloma were not

Table 1 : Clinicopathological profile of the patients

	Patient			Type		Features of Type 1 reaction						
	No	Age	Sex			Dermal edema	Intra-granuloma oedema	GC no size	GC	Vascularty	Neutrophil	BI
GROUP 1	1	12	M	BT	D	+	+	+++	L	+	-	-
	2	33	M	BT	D	+	+	++	L	-	-	-
	3	28	F	BT	D	+	+	+++	L	+	+	-
	4	19	M	BT	D	+	+	++	L	-	-	-
	5	47	F	BB	D	+	+	++	L	+	-	-
	6	38	M	BL	D	+	+	++	M	-	-	+
	7	53	M	BL	D	+	+	-	-	-	+	+
	8	40	M	BT	PR	-	+	++	L	+	+	-
	9	38	M	BL	PR	+	-	++	M	-	-	+
	10	24	F	BL	PR	+	-	++	M	-	-	+
	11	15	M	BL	PR	-	-	++	M	-		+
GROUP 2	12	26	M	BL	PO	+	+	++	M	-	+	+
	13	19	M	BT	PO	+	+	++	L	-	-	-
	14	55	F	BT	A	+	+	++	L	+	-	-
	15	40	M	BT	A	-	+	+	S	-	-	-
	16	50	F	BT	A	+	-	+	M	-	-	-
	17	8	M	BT	A	-	-	-	-	-	-	-
	18	23	M	BT	A	-	-	+	S	-	-	+
	19	15	M	BT	A	-	-	-	-	-	-	-
	20	22	M	BT	A	-	-	+	S	-	-	-
	21	25	F	BT	A	-	-	+	S	-	-	-
	22	30	F	BT	A	-	-	+	S	-	-	-
	23	50	M	BT	A	-	-	+	L	-	-	-

Table 2 : Clinicopathological profile of the patients

	Group 1	Group 2	P value
Epidermal flattening	11(100%)	9(75%)	0.21
Dermal edema	9(81.4%)	4(33.3%)	0.0036**
Intra-granuloma edema	11(100%)	7(58.4%)	0.0373*
Number of giant cells	10(90.9%)	9(75%)	0.5901
Presence of large-medium giant cells	10(87.4%)	5(41.6%)	0.0272*
Presence of neutrophils	3 (17.4%)	1(8.3%)	0.3168
Vascular changes	4(36.36%)	1(8.3%)	0.155
Total no. of patients in group	11	12	

** P value < 0.01

* P value < 0.1

well organized in these cases (Figure 1, 3). In Group 2, 59% of the patients had small giant cells. The granulomas were well organized as compared to Group 1. The number of giant cells (Graded as +/ ++/ +++ by the expert pathologist) was not significantly different between the two groups. Though three cases in Group 1 and one case in Group 2 had few neutrophils, this finding was also not significant.

Vascular changes as evidenced by the dilatation of capillaries and small blood vessels were seen in 4 (36.36%) cases in Group 1 and in one case in Group 2. (Table 1, 2)

Discussion

In our study, only 48% of the clinically diagnosed cases showed histological features suggestive of TIR. The most sensitive parameters in our study were dermal edema, intra-granuloma edema and giant cell size. This is similar to the experience of others in published literature. HLA-DR was not analyzed due to lack of availability. The criteria set out by Lockwood et al seem to have relevance even in our population (Lockwood et al 2008). Documentation of the above mentioned parameters is recommended when reporting histopathology sections of patients suspected to have TIR.

Clinical findings should remain the mainstay of diagnosing TIR. Our sample size is small and larger studies are recommended to propose histological diagnostic criteria for TIR.

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