Our Dermatology Online

Original Article

The scenario of Lepra reaction at the Tertiary Level Hospital in a Hilly State and our experience with its management

Kuldeep Verma, Mudita Gupta, Reena K Sharma

Department of Dermatology, Venereology and Leprosy, IGMC, Shimla, India

Corresponding author: Dr. Mudita Gupta, E-mail: muditadrgupta@yahoo.com

ABSTRACT

Background: Leprosy is a curable disease but, due to the presence of bacilli in the tissues, altered immune response hypersensitivity reactions may develop, which can increase the morbidity rates of the disease. We planned this study to observe the types of leprosy hypersensitivity reactions, their onset, presentation and response to treatment. This retrospective study was conducted over a 2-year period - from January 2015 to December 2016 - to evaluate the scenario of Lepra reaction in Hansen patients in Indira Gandhi Medical College in Shimla, Himachal Pradesh, India. **Results:** A total of 66 patients were registered as new cases of Hansen's disease. Lepromatous leprosy (LL) was the most common spectrum. A total of 41 patients (62.1%) developed a reaction either at presentation or during the course of the disease. Infection as a trigger of the reaction was elucidated in 6 patients, while trauma and vaccination triggered a reaction in 2 patients. Type 1 reaction (T1R) was observed in 18.18% of patients, while type 2 reaction (T2R) appeared in 43.93% of patients. The most common age group for T1R was 30-45 years, while for T2R it was the ages of 15-30. Grade 1 deformity (G1D) was present in 30 patients, grade 2 deformity (G2D) was present in 26 patients, while grade 2 deformity of eyes was diagnosed in 6 patients. A significant number of patients (36.5%) who developed reactions were relieved by the standard World Health Organisation's (WHO) regimen of prednisolone. Adjuvant drugs in the form of clofazimine, thalidomide and methotrexate were given to non-responders. **Limitation:** Due to the short follow up period, we did not observe late reactions. **Conclusion:** In our study, multibacillary leprosy was more common, and the younger age group was involved, thus leading to more deformities, stigma and impaired quality of life. Hansen's disease is a slowly progressive, curable disease, but an interruption by hypersensitivity reactions can alter the course of the disease, which may lead to deformities, hence the need for it to be managed vigorously.

Key words: Leprosy; Lepra reaction; Triggers; Deformities

INTRODUCTION

The causative agent of leprosy, *Mycobacterium leprae*, was identified by Armauer Hansen in 1873 [1]. Leprosy has a predilection for skin and peripheral nerve. Despite being mildly infectious and curable, the course of the disease is often complicated by potential intermittent hypersensitivity reactions called Lepra reactions that may aggravate the nerve damage and lead to deformities and disabilities, something that has been deeply associated with the social stigma connected with the disease [2]. Reactions often cause the symptoms that compel patients to seek medical attention for the first time. Though we have successfully eliminated leprosy from India, with a current prevalence rate of 0.66 in a population of 10000, and an annual new case detection rate of 9.71 in a population of 100,000 [3], Lepra reactions remains the major problem in the management of Hansen patients. A reaction may occur anytime during the course of the illness or after the release from treatment. Therefore it is not only important that the prevalence of leprosy decreases but the control and management of reactions is equally important.

How to cite this article: Verma K, Gupta M, Sharma RK. The scenario of Lepra reaction at the Tertiary Level Hospital in a Hilly State and our experience with its management. Our Dermatol Online. 2020;11(3):238-242.

Submission: 19.06.2020; **Acceptance:** 21.07.2020

DOI: 10.7241/ourd.20203.3

MATERIAL AND METHODS

A retrospective data analysis of all leprosy cases registered at the Department of Dermatology, Venereology and Leprosy of our Institute of the Tertiary Care Hospital, Indira Gandhi Medical College in Shimla, Himachal Pradesh, India that additionally takes care of looking after leprosy patients. The study period lasted from January 2015 to December 2016. The diagnosis of leprosy was based on the Ridley-Jopling classification, which is based on a detailed morphological, bacteriological (Acid Fast Bacilli in lesions/nasal smears), immunological (Lepromin test) and histopathological examination [4]. Also, cases were classified according to the WHO criteria as multibacillary (MB) leprosy if there are more than 6 skin lesions or positive bacillary index (BI) and paucibacillary (PB) if there are less than 5 skin lesions and negative BI [3]. All these diagnosed cases were started on multidrug treatment (MDT) as per the WHO regime. A detailed medical history and physical examination, including general physical examination, vitals, cutaneous, nerve examination, eye, joints, mucosa and other systemic examination were recorded at the first visit and a monthly follow-up until the completion of MDT and a three-monthly one for 2 years after that were also ordered. This information was collected and entered into an excel spreadsheet. All these patients were subjected to a routine haematological and biochemical examination at baseline and every three months till the completion of the therapy. Type 1 reactions were defined as an acute exacerbation, characterised by cutaneous lesions with redness and swelling or acute nerve tenderness with or without motor or sensory loss or just oedema of hands and feet. Type 2 reactions were defined as multiple, tender, erythematous nodules/ plaques with/without neuritis/constitutional symptoms/involvement of other organs such as eyes, testes, joints, or bones [5]. All the diagnosed cases of Hansen's disease were evaluated for the type of reaction, onset, clinical presentation, course of disease, deformities, frequency of occurrence of reactions, triggering factors and management of reactions. All patients with mild reactions were treated with rest and diclofenac in a twice-daily dose. Those with severe reactions were initially treated with 40 mg of prednisolone, followed by 30 mg, 20 mg, 15 mg, 10 mg, and 5 mg. Each dose was given for a period of 2 weeks. Patients who developed reactions after 3 months of the control of the reaction were labelled as recurrent T2R and those who developed a reaction within 3 months were labelled as chronic T2R. Recurrent ENL was managed with the WHO regimen of tapering doses of prednisolone along with clofazimine, a 100 mg dose TDS for 1 month, followed by a BD dose and OD dose for 1 month each [6]. For chronic reactions, thalidomide and clofazimine were started along with prednisolone.

Data analysis

Data were entered into an excel spreadsheet. Statistical analysis was done using Epi info 7.2.2 (the Centre for Disease Control and Prevention). All discrete variables were expressed as percentages or proportions. Continuous variables were presented in Mean ± SD.

RESULTS

Over a period of 2 years, 66 patients were diagnosed with Hanse's disease (Table 1). Males outnumbered females in a ratio of 3:1 (Table 1). The majority of patients were in the spectrum of Lepromatous Leprosy (LL) (48.5%) followed by Borderline Lepromatous (BL) (27.2 %) (Table 1). A reaction was seen in 41 (62.1 %) patients. The time of presentation of these patients is shown in Table 2. The maximum level of patients presented to us with a reaction (65.8%) at the time of the diagnosis of Hansen's. T2R was more commonly observed in 43.93% (Table 3). T1R were the most common in the BL spectrum and T2R in LL disease (Table 3) The patients' history was analysed to find any triggering factors. In most of the cases (80.48%), no triggering factors were present. Tubercular

Table 1: Sex distribution of cases diagnosed as leprosy and spectrum of disease

Group	Male	Female	Total
TT	1		1
BT	9	4	13
BL	11	7	18
LL	25	7	32
Pure neuritic	1		1
Indeterminate	1		1
Total	48	18	66

TT: Tuberculoid leprosy; BT: Borderline Tuberculoid leprosy; BL: Borderline lepromatous; LL: Lepromatous leprosy.

Table 2: Onset of reactions after multidrug treatment

Duration from time of onset	Onset of T1R (No. of patients)	Onset of T2R (No. of patients)
At the time of presentation	10	17
0-3 months	0	1
4-6 months	1	2
7-9 months	0	1
10-12 months	0	4
After getting RFT	1	4
Total	12	29

lymphadenitis in one, respiratory tract infections (RTI's) in two, urinary tract infections (UTI's) in two patients, filariasis in one, post BCG vaccination in one and a roadside accident in one were the only cases with triggering factors. Among the age distribution, the most common age group for T1R was 30-45 years which included 5 patients (41.6%) while the most common age group for T2R was 15-30 years which included 12 patients (41.37%) (Table 4). Regarding the deformity of patients, grade 2 deformity (G1D) of hands and /or feet was quite common (26 patients). Eyes involvement was seen in 6 patients (9.09%). Grade 0 deformity was observed in 10 (15.15%) patients while 84.8 % of patients had some deformity or the other (Table 5).

The management of patients who developed reactions during the course of the disease was also analysed. There were three patients (7.31%) with a mild and 92.6% with a severe reaction. It was observed that 15 patients (36.6%) who developed a severe reaction were relieved with a single course of tapering steroids as per the WHO schedule. Poor compliance and interruption of steroid therapy with a subsequent Lepra reaction was observed in 13 (31.7%) patients. Recurrent T2R was seen in 8(19.5%) patients. Out of these cases of the recurrent reaction, 5 (12.1%) cases reported improvement with no further reaction episodes with prednisolone and clofazimine tapering doses, while in 3 (7.3%) cases thalidomide had to be added. There were 3 (7.3%) patients with chronic T2R.

Table 3: Prevalance of reaction

Type of leprosy	T1R	%	T2R	%
TT	1	1.51	-	
BT	4	6.06	3	4.54
BL	7	10.60	11	16.67
LL	-		15	22.73
Total	12	18.18	29	43.93
Grand total	41 out of 66 patients (62.12%)			

TT: Tuberculoid leprosy; BT: Borderline Tuberculoid leprosy; BL: Borderline lepromatous; LL: Lepromatous leprosy.

Table 4: Age distribution of reaction

Age (years)	Type 1		Total	Type 2		Total
	Male	Female		Male	Female	
0-14	0	0	0	0	0	0
15-30	3	0	3	6	6	12
31-45	4	1	5	8	0	8
45-60	1	0	1	5	0	5
>60	3	0	3	3	1	4
Total	11	1	12	22	7	29

Table 5: Type of deformity

Type of deformity	No. of patients	Prevalence
Grade 1	30	45.45
Grade 2	26	39.39
Grade 2 eyes	6	9.09

DISCUSSION

Leprosy is a disease known for its low infectivity and chronic course. Although it appears to be a benign infectious disease, it is often complicated by immunologically mediated hypersensitivity reactions called Lepra reactions which may lead to greater inflammation and damage. Three types of Lepra reactions can be recognized, T1R, T2R and Lucio phenomenon. Risk factors for T1R are a borderline group of patients, patients with previous episodes of reactions, female, of old age, patients with multiple or disseminated patches or large facial patches, starting with MDT which can lead to a breakdown of Bacilli and release of bacterial antigens, immunotherapy and the hepatitis B or C infection [2]. Clinically T1R can be observed as erythema, oedema and tenderness of a pre-existing lesion associated with nerve tenderness and oedema of extremities. Risk factors for T2R are LL with skin infiltration, anti-leprosy drugs except clofazimine, bacteriological index (BI)>4, age < 40 years, intercurrent infections, trauma, surgical intervention, stress, immunization, pregnancy, parturition, and drugs like potassium iodide. T2R reaction is characterized by the sudden appearance of crops of evanescent pink coloured tender papules, nodules or plaques variable in size. These skin lesions are known as Erythema Nodosum Leprosum (ENL). ENL lesions are associated with systemic complaints in the form of a fever, myalgia, arthralgia, orchitis, ocular complaints etc. Lucio phenomenon is a rare form of Lepra reaction observed in Lucio leprosy [2]. It can be characterized by slightly indurated red-bluish plaques on the skin with an erythematous halo which may later develop into a necrotic eschar which detaches easily to reveal an irregularly shaped ulcer but patients remain afebrile. NLEP guidelines on reactions have clearly differentiated between mild and severe T1R, T2R, as well as basic differences between the two types of reaction [7].

Implementation of MDT has brought a decline in the incidence of reactions. Vijaya Kumaran et al. in their study observed a fourfold reduction in the incidence of late Lepra reactions in patients who received MDT *versus* patients only undergoing dapsone monotherapy [8].

Age and sex distribution of our study compared to other studies is displayed in Table 6 [9-13]. As shown in Table 6, the most common age group involved in most of the studies was 20-40 year. This could be because this age group, being the most physically active group, is more prone to get in contact with leprosy patients and to develop reactions. Ortiz et al observed that only 2.98% of patients were in the paediatric age group.[14] In our study, the majority of patients were in the spectrum of Lepromatous Leprosy (LL) which is in contrast to other studies, except the one in our state. Other studies from our and neighbouring country observed BT to be the most common [9-11]. The reason could be that cases of BT Hansen's are more easily recognized and managed at the periphery while difficult cases were referred to our tertiary health centre. Another reason is that our state is a hypo-endemic area for Hansen's disease so LL patients dominated. Puri et al also observed multibacillary leprosy to be more common (75.6% versus 24.4%). [15]

In our study, the overall prevalence of Lepra reaction was 62.12%. Out of total leprosy patients, 41% of patients (65.8% of total patients with reactions) had a reaction at the time of diagnosis and 7.5 % developed it after stopping MDT. Most of the other studies, as shown in Table 6, have reported a much lower incidence of leprosy reactions [9-12]. Sharma et al reported 51.6% patients of T1R and 76. 5 % of T2R were in a reaction at the time of diagnosis.[9] In our case, most of T1R first had a reaction at the time of diagnosis (83.3 %) while only 58.6 % in T2R. Similarly, in a study by Sallodkar and Kalla [13], 33% of the patients presented with a reaction during their first visit while Brakel et al [16] observed that 59% of their patients had T1R at presentation. Similarly, Manandhar et al, in their study of reactions, observed that 34% of the patients had T2R at the time of presentation, 32% developed it within 6 months and 19% - after one year of treatment [17]. The higher rate of reaction cases in our centre may be due to difficult terrain, physical exertion and more. Also, most of our patients belonged to the financially challenged socio-economic group, migrant labourers, who only presented when they were symptomatic. Also, we had a greater number of patients displaying type 2 reaction, compared to other studies. This could be because of a greater number of multibacillary patients in our study.

In our study, T1R was seen in the maximum BL>BT>TT (10.60%,6.06%,1.51% respectively). Sharma et al had the maximum prevalence of T1R in BB>BL>BT>LL (23.3%, 18.18%, 6.25%, 3.25% respectively) [9]. Brakel et al also observed the maximum T1R in BT Hansen> BL (34.15%,30.6% respectively) [16]. In our study, the relatively higher incidence of T1R in BL could be because we had a greater number of patients in the BL spectrum and no patient in BB.

In our study, the highest prevalence of T2R was found in LL >BL>BT (22.73%,16.67%,4.54%). The findings were similar to Sharma et al [9] where the frequencies of T2R in LL and BL patients were 22.8% and 4.5% respectively, with LL patients having a significantly higher value than BL patients. Brakel et al also observed a similar pattern [16]. The high bacillary load in LL predisposes the patient to type 2 reaction.

In our study, 80.48 % of patients had no specific triggering factor. Similarly, in a study by Prasannan et al, no triggering factor was identified in 80-84 % of patients in T1R and T2R [18].

A timely management of reactions is very important in preventing the progression of sensorimotor deficit and the subsequent development of deformity. We had a high incidence of deformities in our patients, which can be because of a high percentage of patients presented with reactions and also non-compliance with the treatment of reactions since recurrent and chronic reactions increase the risk of deformities.

Lepra reactions are managed predominantly with the help of corticosteroids, thalidomide, clofazimine, and steroid-sparing agents like methotrexate, azathioprine, cyclosporine, mycophenolate mofetil etc [6]. Prednisolone and thalidomide prove effective

Table 6: Comparison of various parameters in different studies

Study	Sex M:F	Age group maximum involved (years)	Commonest spectrum	Reaction (%)	Type 1 (%)	Type 2 (%)
Ours	2.66:1	T1R (30-45) T2R (15-30)	LL (48.48)	62.12	29.26	70.7
Sharma [9]	2.79	-	BT (63.7)	12.8	63.3	36.7
Chhabra [10]	2.3	21-40	BT (56.3)	37.5	81.06	19.7
Singh [11]	2.08	-	BT (32.9)	14.6	57.6	43.4
Jindal [12]	3	20-40 (47.8%)	LL (33.12)	-	-	-
Salodhkar [13]	2.42		Polar leprosy (50)	11	19.2	80.1

LL: Lepromatous leprosy; BT: Borderline Tuberculoid leprosy.

in the management of acute reactions. A long-term use of prednisolone, which may be required in the control of reactions, may lead to steroid-induced side effects and a recurrence of lesions after the withdrawal of steroids. Clofazimine has to be added in recurrent and chronic reactions because of its deposition in the reticuloendothelial system and macrophages, which interferes with the capacity of macrophage to process and present antigens, thereby preventing their mobilization and activation, and Interleukin-2 release.

Limitation

Due to the short follow up period, we could not find the true incidence of late reactions. Secondly, because the patients were coming from remote areas, the standard dose schedule of prednisolone at the referral centre given by Girdhar et al. [18] was not followed. Thirdly, the poor financial condition of the patients restricted us in using thalidomide or other steroid-sparing agents in the majority of patients.

CONCLUSION

In the end, we can conclude that leprosy, though it is a benign and chronic disease, it is very commonly interrupted by reactions which can be more damaging than the disease itself. The recognition of warning signs of a reaction is very important. Deformities can be prevented by early diagnosis and prompt treatment of these reactions.

Statement of Human and Animal Rights

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Statement of Informed Consent

Informed consent was obtained from all patients for being included in the study.

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Source of Support: Nil, **Conflict of Interest:** None declared.