Research Paper

Volume : 2 | Issue : 1 | Jan 2013 • ISSN No 2277 - 8179

Medical Science

KEYWORDS : Lepra Reactions, Enl, Neutrophilic Infiltrate.

# Lepra Reactions-A Clinical & Histopathological Study

| | |
|---|---|
| Dr. Neha Sharma | 3rd Year Post Graduate Student, Smt. S.C.L Hospital, Ahmedabad |
| Dr. Neela M. Patel | Associate Professor, Smt. S.C.L Hospital, Ahmedabad |
| Dr. Nirali Mahakal | 2nd Year Post Graduate Student, Smt. S.C.L Hospital, Ahmedabad |

## ABSTRACT

*Reactions are immunologically mediated episodes of acute & sub-acute inflammation which interrupt, the relatively uneventful course of leprosy. The objectives of the present research are to study the epidemiology, precipitating factors, clinical features, routine investigations(Ix) and histopathological features of lepra reactions. Among the 364 leprosy patients, 156(42.8%) had reactions at any point in their disease ,type 1(T1R) in 71.8% and type 2(T2R) in 28.2%. 61.5% males and 10.2% females had T1R while 16.6% males and 11.5% females had T2R.Maximum incidence of reactions was in 21-40 year age groups and in borderline leprosy patients.4.5% patients with T2R had recurrent ENL for years even after successful treatment. Commonest precipitating factors were intercurrent infections in 45.5% T1R, 43.2% T2R and stress in 16% T1R, 22.7% T2R patients. Sudden exacerbation of pre-existing skin lesions and/or appearance of new lesions in 150(96.1%) and nerve involvement in 80(51.3%) patients. Skin biopsy of T1R patients showed histological upgrading in 46.2%, downgrading in 10% and T2R patients showed dermal edema in 74.4%,neutrophilic infiltrate in background of macrophage granuloma and vasculitis in 2.1%. Histopathology has a diagnostic as well as prognostic significance.*

**INTRODUCTION:**

Leprosy is a chronic disease which progresses very slowly. However, during its long course complications like reactions may occur. Reactional states are a central problem in Hansen's disease. To the patient, they are a major source of morbidity. To the clinician, they are a therapeutic challenge. To the investigators, they are a window of opportunity for the study of immune regulation and perhaps, the mechanisms leading to silent nerve destruction. Conceptually, reactional states are easier described than defined. They represent several types of host responses which are superimposed as it were, on the underlying granulomas. In a reactional state, the excited, energised granuloma can injure tissues in ways it might not when not in reaction; eg. Producing nerve trunk palsies or iritis.1 nerve damage lies at the root of many of leprosy's problems, as deformities are almost entirely secondary to damage of peripheral nerves, resulting in misuse and infection. Thus lepra reactions are emergencies which are unpredictable, progressive, possibly irreversible yet potentially treatable and are a serious problem in modern leprosy, particularly considering that patients are already under treatment. The incidence of leprosy in India at present is estimated at 2.4 million2

**MATERIALS AND METHODS:**

The study was conducted on 164 patients of lepra reaction. All patients who were in reaction during the period of study and attending the out patient department of the hospital were included. A detailed history including skin lesions, associated systemic complaints, precipitating factors for the reaction was taken. Past history, personal history and obstetric history in females was noted. Detailed clinical examination was done including general examination, systemic examination, skin examination, sensory testing, motor testing, nerve examination, eye examination, skeletal examination and genital examination in males. Presence of deformity of nose, mouth, face, hands and feet was noted. The gait of the patient was observed. The patient was examined for the presence of trophic ulcers. All patients were advised to undergo routine investigations. Slit skin smear examination was done in all patients from the margin of the patch and another smear from the ear lobule. The smears were stained by Zeihl-neelson's staining and BI and MI were determined. A skin biopsy was taken and sent for H&E and AFB staining.

**RESULTS:**

61.5% males and 10.2% females had T1R while 16.6% males and 11.5% females had T2R. (TABLE-1). 75.6% of patients of reactions were in 21-40 year age group. (TABLE-2) and in borderline leprosy patients. (TABLE-3) Commonest precipitating factors were intercurrent infections in 45.5% T1R, 43.2% T2R and stress in 16% T1R, 22.7% T2R patients. Among the systemic findings, 10.2% patients had low grade fever and 9% had peripheral edema, 8% had lymphadenopathy and 6.5% had eye involvement.Sudden exacerbation of pre-existing skin lesions and/or appearance of new lesions in 150(96.1%) and nerve involvement in 80(51.3%) patients.Skin biopsy of T1R patients showed histological upgrading in 46.2%, downgrading in 10% (TABLE-4) and T2R patients showed dermal edema in 74.4%,neutrophilic infiltrate in background of macrophage granuloma and vasculitis in 2.1%.(TABLE-5)

**Table-1**

| sex | type 1 reaction | | type 2 reaction | |
|---|---|---|---|---|
| | number of patients | percentage (%) | number of patients | percentage (%) |
| male | 96 | 86 | 26 | 59 |
| female | 16 | 14 | 18 | 41 |
| total | 112 | 100 | 44 | 100 |

**Table-2**

| Age | type 1 reaction | | type 2 reaction | | total | |
|---|---|---|---|---|---|---|
| | number | percentage(%) | number | percentage(%) | number | percentage(%) |
| 0-10 | 1 | 1 | 0 | 0 | 1 | 1 |
| 11-20 | 7 | 7 | 3 | 7 | 10 | 7 |
| 21-30 | 46 | 41 | 20 | 45 | 66 | 42 |
| 31-40 | 40 | 36 | 12 | 27 | 52 | 32 |
| 41-50 | 10 | 10 | 3 | 7 | 13 | 8 |
| 51-60 | 3 | 3 | 5 | 11 | 8 | 7 |
| >60 | 5 | 5 | 1 | 2 | 6 | 3 |

**Table-3**

| type of leprosy | type 1 reaction | | type 2 reaction | | total | |
|---|---|---|---|---|---|---|
| | no. | % | no. | % | no. | % |
| Tt | 0 | 0 | 0 | 0 | 0 | 0 |
| Bt | 36 | 32 | 0 | 0 | 36 | 23 |
| Bb | 31 | 28 | 0 | 0 | 31 | 20 |
| Bl | 45 | 40 | 20 | 45 | 65 | 42 |
| Ll | 0 | 0 | 24 | 55 | 24 | 15 |
| Total | 112 | 100 | 44 | 100 | 156 | 100 |

**Table-4**

| histological features | number of patients | percentage (%) |
|---|---|---|
| lymphocytes in granuloma | 10 | 9 |
| edema in papillary dermis | 45 | 40 |
| edema within granuloma | 52 | 46.2 |
| lymphocytes at interface | 4 | 4 |
| giant cells | 52 | 46.2 |

**Table-5**

| histopathological features | number of patients | percentage (%) |
|---|---|---|
| neutrophils within granuloma | 1 | 2.1 |
| edema in papillary dermis | 33 | 74.4 |
| fibrin in vessel wall | 1 | 2.1 |

**DISCUSSION:**

Lepra reactions are immunologically mediated episodes of acute and subacute inflammation which interrupt, the relatively uneventful usual chronic course of disease affecting the skin, nerves, mucus membranes and/or other sites. The type 1 reaction is associated with sudden alteration of cell-mediated immunity associated with a shift in patient's position in the leprosy spectrum, usually observed in borderline spectrum of the disease.3 Type 2 reaction is an immune complex syndrome(antigen-antibody reaction involving complement). It is an example of type III hypersensitivity reaction (Coombs and Gell classification) or Arthus phenomenon. IgG, IgM, complement (C3) and mycobacterial antigens are all identified at the site of erythema nodosum leprosum(ENL). They occur mostly in lepromatous (LL) and sometimes in borderline-lepromatous leprosy(BL). The present study shows 42.8% patients of leprosy show reaction at any point in their disease which is much more than the incidence of 2.07% reported by B. Debi et al. The explanation for this could be that main referral centres may report a high frequency from the very nature of the patients which attend there. Type 1 reaction was the commonest reaction encountered, nearly three times more commonly than type 2 reaction. This could be accounted for by the decreasing number of patients in lepromatous leprosy due to multi drug therapy and intense control work.4 There was higher incidence of reactions in males which can be attributed to the higher incidence of leprosy among males than in females. 75.6% of patients with reactions were in age group 21-40 years in contrast to the commonest age group of 41-60 years reported by Debi and Mohanty.5 The frequency of reactions was found to be maximum in borderline spectrum unlike that reported by V.N.Sehgal et al where highest frequency was in lepromatous leprosy.6Intercurrent infections were the most frequent precipitating factors. They probably affect the immunity of the body either cell mediated or humoral. An intercurrent viral infection, by inducing interferon production, could allow activation of otherwise quiescent antigen presenting cells.7 Physical and mental stress were implicated as the next commonest precipitating factors. Paul Klerenman states that stress is an immunostimulant and that two pathways may be of importance: 'hardwiring' to lymphoid tissue, spleen etc. From the nervous system, and humoral links through a remarkable number of shared chemical transmitters (eg. endorphins, substance P) which may act in both directions, making the immune system a 'mobile brain'.45 Exacerbation of the pre-existing lesions either alone or in combination with new lesions was the commonest presenting feature.8 (FIGURE-1) The new lesions presumably develop due to immunological recognition of inapparent foci of M. Leprae.9 Nerve involvement in the form of nerve thickening, tenderness and abscess formation was noted in 51.3% patients. Low grade fever in 10.2% patients could be associated with a marked enhancement of cell mediated immunity. Peripheral edema which was pitting and non-tender was present mainly in BL and LL patients. (FIGURE-2) Eye involvement in the form of ciliary/supraciliary madrosis, lagophthalmos, exposure keratitis and iridocyclitis was seen in 6.5% patients. In the skin biopsy of T1R patients, most of the patients showed histological upgrading, while T2R patients showed dermal edema and neutrophilic infiltrate in background of macrophage granuloma as the commonest histopathological findings. Ridley has described the features of upgrading as formation of whorls/ nests of epitheloid cells, giant cell formation, edema of dermis and erosion of epidermis by granuloma in some cases.10(FIGURE-3) Downgrading is suggested by diffuse macrophage cell infiltrate, few lymphocytes, inconspicuous giant cells with dermal edema.11 Type 2 reaction patients showed atrophic epidermis, well formed grenz zone (FIGURE-4)and thickening of vessel wall with polymorphonuclear infiltrate around the blood vessels. Extravasation of RBCs was seen in some slides.

**FIGURE-1**

**FIGURE-2**

**FIGURE-3**

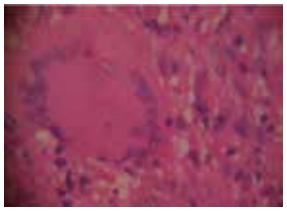
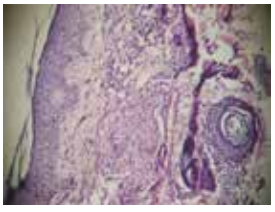


**FIGURE-4**



**CONCLUSION:**

Early diagnosis of reactions and recognition of the precipitating factors can be very helpful in preventing disability and deformity. Histopathology has a diagnostic as well as prognostic significance.

## REFERENCE

1) Lever WF- Leprosy in ' Histopathology of skin'. 7th ed. Pg.337. JB. Lippin Cott Company. | 2)International Leprosy Union (1992) Jan, Issue No. 6 Pg.6. | 3)Kar BR, Job CK.Very rare reversal reaction and Mitsuda Conversion in secondary Lepromatous Leprosy, A case report.Lepr Rev 2005,76:258-62. | 4) Gillbody JS- Impact of Multidrug therapy on the treatment & control of leprosy. Int.J.Lepr, 1991;59:456-478. | 5) Deb i B & Mohanty HC React i ona I s ta tes of I eprosy ~ Lepr. India, 1977; 49:229 | 6) Sehgal VN, Rege VL at al- Pattern of reactions in leprosy. Lepr India, 1977; 49:221. | 7) Paul Klenerman Etiological factors in delayed type hypersensitivity reactions in leprosy. Int.J.Lepr, 1987; 55:702-712 Petit JHS, Waters MFR Lepr, 1967; 35:1-10. | 8) Sehgal VN, Rege VL at al- Pattern of reactions in leprosy. Lepr India, 1977; 49:221. | 9) Patricia Rose & MFR Waters- Reveasal reactions in leprosy and their management. Lepr Rev.,1991;62;113-121. | 10) Dharmendra Leprosy Vol.2 (1985) Samant and company. Ridley OS Skin biopsy in leprosy, 1977; 147-151 Oocumenta Giegy Publication. Ridley OS & Radia KB The histological course reactions in Borderline Leprosy and their outcome. Int.J.Lepr,1981; 49:383-392. | 11) Dharmendra Leprosy Vol.2 (1985) Samant and company. Ridley OS Skin biopsy in leprosy, 1977; 147-151 Oocumenta Giegy Publication. Ridley OS & Radia KB The histological course reactions in Borderline Leprosy and their outcome. Int.J.Lepr,1981; 49:383-392. Mukherjee A & RS Misra- Comperative histology of skin and nerve granulomas in leprosy Patients, Lepr Rev., 1988;59;177-180. |