

Lepra reactions in new leprosy cases at diagnosis: A study of 50 Pakistani patients

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Abstract

Objective: To determine the occurrence and characteristics of the two types of lepra reactions in new leprosy cases at initial diagnosis.

Method: The retrospective descriptive study was conducted at the Marie Adelaide Leprosy Centre, Karachi, and comprised all new leprosy cases registered from January 1, 2016, to June 30, 2018. Data was collected from the medical record database using a predesigned proforma.

Results: Of the 50 cases, 2(4%) were children and 48 (96%) were adults, with overall age ranging from 12 to 85 years. There were 41 (82%) males and 9(18%) females.. Of the total, 30(60%) cases presented with type 1 reaction and 20(40%) with type 2. Further, 30(60%) cases were classified as borderline lepromatous. Among them, 17(57%) had type 2 reaction. Inflamed plaques were the main feature in 27(90%) cases of type 1. Crops of painful, erythematous nodules were seen in 19(95%) cases of type 2.

Conclusion: Lepra reactions were found to be a presenting feature in a significant number of new leprosy cases at initial diagnosis.

Keywords: Leprosy, Lepra reactions, Type 1 (reversal) reaction, Type 2 erythema nodosum leprosum reaction, ENL.
(JPMA 71: 838; 2021) DOI: <https://doi.org/10.47391/JPMA.878>

Introduction

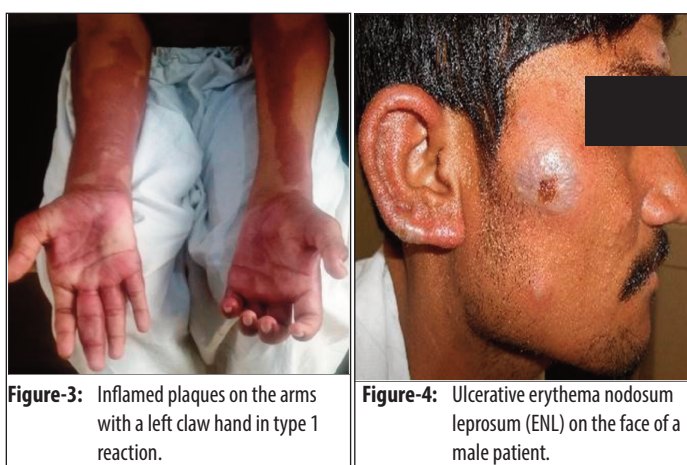
Hansen's disease (HD), also called leprosy, is a curable infection that remains endemic in more than 140 countries around the world. Despite having been declared as a globally eliminated issues alongside 51 public health problems by the World Health Organisation (WHO), a large number of new cases have been reported.¹ These are mainly of two types; type 1 (reversal), and type 2 erythema nodosum leprosum (ENL) (Figures 1-4). The former are caused by a delayed-type hypersensitivity to bacillary antigens and occur in the borderline types of the disease, which are immunologically unstable; borderline tuberculoid (BT), mid-borderline (BB) and borderline lepromatous (BL). The latter happens to be an immune complex disorder and occur in BL and lepromatous leprosy (LL).²

Reactions are characterised by an acute inflammation in lesions. In type 1 reactions, there is redness, swelling and sometimes tenderness of skin lesions and swelling, pain and tenderness of nerves, often accompanied by loss of function. New lesions may appear. Lesions of type 2 reactions tend to appear in crops, new ones appearing as the old ones subside, every few days. They present as small papules or large nodules, which may be superficial or deep

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and may be painful and tender. Neuritis may occur together with skin lesions or independently, in a type 1 reaction and is often less marked in type 2 reactions. The latter are often accompanied by a systemic illness with a high fever. Uveitis, myositis, arthritis, lymphadenitis and orchitis can be the other manifestations of a type 2 reaction.² Leprosy reactions can occur before, during or after the completion of anti-leprosy, multi-drug therapy (MDT) and can be frequently recurrent.^{3,4}

The current study was planned to determine the occurrence and characteristics of the two types of leprosy reactions in new leprosy cases at initial diagnosis.

Patients and Methods

The retrospective descriptive study was conducted at the Marie Adelaide Leprosy Centre, Karachi, and comprised all new leprosy cases registered from January 1, 2016, to June 30, 2018. After approval from the institutional ethics review committee, the sample was raised using non-probability convenience sampling technique. Informed written consent was taken from all the patients after reassuring them about anonymity of data. Medical records were checked and all cases who had presented with either a type 1 or type 2 reaction at the time of diagnosis were included. Cases who had not presented with a leprosy reaction at initial diagnosis were excluded, and so were those who presented with a reaction after starting anti-leprosy treatment.

Data was collected on a predesigned proforma related to medical histories, physical examination records and laboratory investigation reports.

Results

Of the 50 cases, there were 41(82%) males and 9(18%) females; and 2(4%) were children and 48(96%) were adults. The overall age range was 12-85 years, with the highest number of cases being in the 45-54 age-group 13(26%), followed by 11(22%) aged 25-34 years.

Of the total, 30(60%) cases presented with type 1 reaction Group A and 20(40%) with type Group B. The age range in Group A was 12-76 years, with 18(60%) aged 25-54 years. The age range in Group B was 19-85 years, with 15 (75%) aged 25-54 years.

In Group A there were 22(54%) males, and in Group B there were 19(46%). Among females, 8(89%) were in Group A and 1(11%), in Group B.

Of the total, 39(78%) cases were residents of Sindh, followed by 8(16%) from Balochistan, 2(4%) from Punjab and 1(2%) from Azad Jammu and Kashmir (AJK). Among the cases from Sindh, 30(60%) were residents of Karachi.

Urdu, Sindhi and Balochi were the most common languages spoken; being the mother-tongue of 11(22%) cases each. Pushto was spoken by 5(10%), Seraiki by 4(8%), Hindko by 3(6%) and Punjabi by 2(4%). Brahvi, Chitrali and Katchi were represented by 1(2%) case each.

None of the cases was classified as tuberculoid (TT) (Table 1). A total of 5(10%) cases were classified as BT and all were in Group A. One (20%) of these had ulnar neuritis. Overall, 12(24%) cases were classified as BB and all were in Group A, with 5(41.6%) of them being mild.

BL was identified in 30(60%) cases; 13(43%) in Group A and 17(57%) in Group B. In Group A, 2(15.4%) cases had a mild reaction and 3(23%) presented with predominant neuritis. In Group B, 1(6%) had ulcerative ENL. Overall, 3(6%) cases were classified as LL and all were in Group B, with 1(33%) having an ulcerative presentation.

In 27(90%) Group A cases, the main presentation was inflamed plaques on face, limbs and trunk. The duration ranged from one week to two years. In 5(16.6%) cases with mild reaction, there was a flare-up within one week to two months of starting anti-leprosy MDT. In 1(12.5%) female patient, the reaction occurred 6 days after delivery.

In 10(33%) Group A cases, the reaction was confined to skin lesions. In 16(53%) cases, both skin and nerves were involved. Anaesthesia was detected in skin lesions of 18(60%) cases in Group A and punched-out plaques were seen in 16(53%).

In Group B, 19(95%) cases presented with crops of painful, erythematous nodules on the skin. Duration varied from 1 week to 7 years. In 2(10.5%) cases, there was a history of similar episodes 6-10 months earlier. Papules were seen in 4(21%) cases, pustules and plaques in 2(10.5%) cases each, 3(16%) had ulceration and 1(5.2%) presented with diffuse infiltration. In 12(60%) Group B cases, both skin and nerves were involved.

The supra and infra-orbital branches of the trigeminal nerve were found to be enlarged in 1(3.3%) Group A patient, and 1(3.3%) case presented with a lagophthalmos due to facial nerve involvement. Great auricular nerve was enlarged in 6(20%) cases of Group A and 1(5%) of Group B.

Ulnar nerves were found to be enlarged in 22(73%) Group

Table-1: Distribution of cases according to classification.

Classification	Type 1 reaction	Type 2 reaction	n (%)
Tuberculoid	0	0	0
Borderline tuberculoid	5	0	5 (10)
Mid-borderline	12	0	12 (24)
Borderline lepromatous	13	17	30 (60)
Lepromatous leprosy	0	3	3 (6)

A and 12(60%) Group B cases. In Group A, 15(11(50%)) had bilateral enlargement and 11(50%) had asymmetrical enlargement. In Group B, 10(50%) cases had bilateral enlargement and 2(10%) had it asymmetrical.

Radial cutaneous nerve was enlarged in 11(37%) Group A and 11(55%) Group B cases. Common peroneal nerves were enlarged in 15(50%) Group A and 13(65%) Group B cases. Bilateral enlargement was seen in 12(40%) Group A and 12(60%) Group B cases. Posterior tibial nerves were found enlarged in 18(60%) Group A and 11(55%) Group B cases.

In 2(7%) Group A cases, the presentation was that of neuritis without any inflamed skin lesions. Also, 2(7%) cases in Group A and 3(15%) cases in Group B had no enlarged nerves (Table 2).

Anaesthesia in hands or feet was detected in 17(57%) Group A and 6(30%) Group B cases. Glove and stocking pattern was seen in 3(10%) Group A cases and 1(5%) Group B case.

Muscle weakness was found in 12(40%) Group A cases; 1(3.3%) had lagophthalmos and 5(17%) had claw hands. One (3.3%) case presented with a wrist drop and the same patient, together with another, 2(7%) also had a foot drop. In Group B, muscle weakness was found in 8(40%) cases; 2(10%) had claw fingers and 1(5%) had claw toes (Table 3).

Fever was the presenting complaint in 16(80%) Group B and 6(20%) Group A cases. Duration of fever in Group B ranged from two days to one-and-a-half year. Of the 16 cases with ENL, 8(50%) had rigours accompanying the

Table-2: Nerve involvement in the 2 types of reactions.

Enlarged nerves	Type 1 reaction n (%)	Type 2 reaction n (%)
Supraorbital	1 (3)	0
Infraorbital	1 (3)	0
Ulnar	22 (73)	12 (60)
Radial Cutaneous	11 (37)	11 (55)
Common Peroneal	15 (50)	13 (65)
Posterior Tibial	18 (60)	11 (55)

Table-3: Signs of nerve damage.

Enlarged nerves	Type 1 reaction n (%)	Type 2 reaction n (%)
Anaesthesia in hands or feet	17 (57)	6 (30)
Glove and stocking anaesthesia	3 (10)	1 (5)
Muscle weakness	12 (40)	8 (40)
Lagophthalmos	1 (3)	0
Claw hands	5 (17)	2 (10)
Wrist drop	1 (3)	0
Foot drop	2 (7)	0
Claw toes	0	1 (5)

fever. The duration of fever in Group A ranged from one week to three months, and 1(3.3%) case complained of rigours.

Pain in limbs was reported by 13(43%) Group A cases and 10(50%) Group B cases. Joint pain was reported by 7(23%) Group A and 6(30%) Group B cases.

Nasal stuffiness was reported by 10(50%) Group B and 5(17%) Group A cases. Epistaxis was a feature in 5(25%) Group B cases with an ENL reaction, and the duration of nasal symptoms ranged from two weeks to four years, with 1(20%) patient's attendants complaining of foul smell from the patient's nose.

Odoema feet was a finding in 7(23%) cases in Group A and 7(35%) cases in Group B. Ulcers were found in the hands and feet of 3(10%) Group A and 2(10%) Group B cases. Submandibular lymph glands were found to be enlarged in 1(3.3%) Group A case, while cervical, axillary and inguinal glands were enlarged in 3(15%) Group B cases. Orchitis was a complication in 3(15%) Group B cases and 1(33.3%) of them also had gynaecomastia.

Also, 4(20%) Group B cases presented with madarosis; 1(5%) had a nasal and a minor septal perforation.

Skin smears were positive for acid-fast bacillus (AFB), in 7(23%) Group A and 13(65%) Group B cases. The range was 0.2+ to 0.8+ in Group A, and 0.2+ to 3.2+ in Group B. In 5(10%) cases, the bacteriological index (BI) was >1+ and all belonged to Group B. BI was negative in 20(67%) Group A and 7(35%) Group B cases. Results were not available for 3(10%) Group A cases.

Histopathology was done in a total of 16(32%) cases. Of these, 7(43.5%) presented clinically as a type 1 reaction and 9(56.5%) as type 2. Among smear negative cases with type 1 and type 2 reactions 3(13%) and 4(57%) cases were found to have AFB on histopathology.

In 1(2%) elderly patient classified as LL with ulcerative ENL, the skin smear was negative but his skin biopsy confirmed LL leprosy and a lymph node biopsy reported ENL reaction. In 1(2%) clinically BB case, the histopathology was suggestive of TT leprosy and no AFB was found in the dermis. In another 1(2%) BB case with a positive smear, histopathology reported features of LL leprosy. In 2(4%) BL cases with ENL, findings indicated ENL histology. In 1(2%) BL case, both skin and lymph node biopsies reported LL leprosy.

Epidermal atrophy, grenz zone formation, foamy macrophages and a positive lepra stain were common histopathological features in Group B, and perivascular infiltrate and neutrophils were also seen in such cases.

Periadnexal and perineural infiltrate with a positive lepra stain were frequent findings in Group A.

History of a household contact was available in 13(43%) Group A and 4(20%) Group B cases.

Delay in diagnosis ranged from 2 weeks to 8 years in Group A, and from 2 weeks to 7 years in Group B.

Discussion

In the current study, 30(60%) cases presented with a type 1 reaction and 20(40%) with type 2. These findings are similar to those of a study done in eastern India with a similar sample size.⁵

In the current study, 30(60%) cases were classified as BL, followed by 24% BB, 10% BT and 6% LL. The proportion of BL cases was higher in both the groups. In a study done in western Nepal, BT was the more common classification in those with type 1 and LL among those with type 2 reaction.⁴ A study in Ethiopia reported a higher proportion of BL cases with a reversal reaction at diagnosis and a higher proportion of LL among those with ENL.⁶

Both skin and nerves were affected in 16(53%) cases with a type 1 reaction and in 12(60%) cases with type 2. In a study done in southern India, both skin and nerves were involved in a higher proportion of type 1 cases (44.4%) compared to type 2 (33.3%).⁷

Ulnar nerves were the most commonly enlarged nerves, in those with type 1 (73%) and common peroneal in type 2 (65%). Facial, ulnar and common peroneal nerves are considered to be most at risk in type 1 reactions.⁸ Anaesthesia in hands and feet was detected in 57% type 1 cases and 30% of type 2. Muscle weakness was found in 40% cases of each type. Claw hand was a presentation in 17% patients of type 1 and in 10% of type 2. In a study from northern India, 39.3% cases had a deformity at the time of diagnosis.⁹ A retrospective study reported 23.3% cases with a claw hand.¹⁰

Fever was a complaint in 80% cases of type 2 and in 20% of type 1, while lymphadenopathy was seen in 3(15%) cases of type 2 and an equal number presented with orchitis. Prasannan et al. reported fever and myalgia in all cases with type 2.⁷ A case report described a young Pakistani male admitted to a rheumatological unit in the United Kingdom with fever, night sweats and an acute polyarthritis. His skin biopsy had revealed lepromatous leprosy.¹¹ In a recently published case report, a 1.5-month history of high-grade fever was reported with uveitis, lymphadenopathy and arthritis in a young Pakistani male, who was later diagnosed as a case of BL leprosy with ENL.¹²

Anaemia, leucocytosis, high erythrocyte sedimentation rate (ESR), and AFB-positive skin smears were also more marked in those with a type 2 reaction. Five cases had a bacteriological index >1+ and all belonged to the type 2 group. Lepromatous leprosy and a higher BI have been identified as risk factors for developing type 2 reactions.¹³ Three and four cases each, among smear-negative type 1 and type 2 were found to have AFB on histopathology. Lockwood et al.¹⁴ illustrated in their cohort study that the classification and diagnosis of leprosy reactions can be complex and it is important that clinicians and pathologists regularly discuss and review patients and their biopsies.

Conclusion

Lepra reactions can be a presenting feature in a significant number of new leprosy cases at initial diagnosis. It is important for healthcare providers, especially dermatologists, neurologists and those dealing with infectious diseases, to have knowledge about the signs and symptoms of both types of reactions to ensure early detection and treatment. This can help in preventing disease transmission, as well as the occurrence of deformity and disability.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

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