

Clinical profile of patients with pure neuritic leprosy: 20 years' experience at a tertiary referral centre from North India

Mala Bhalla^{a, †}, Kavita Poonia^{a, †}, Surbhi Jain^a,
Gurvinder Pal Thami^a & Priyanka Sharma^a

^aDepartment of Dermatology, Venereology and Leprology, Government Medical College and Hospital, Sector-32, Chandigarh-160012, India

Submitted 22 January 2022; Accepted 27 April 2022

Summary

Introduction Pure neuritic leprosy (PNL) is characterized by enlargement of peripheral nerves, sensory loss without any cutaneous lesions, skin slit smear negativity and a variable lepromin test and histopathology.

Methods This was a retrospective analysis of the clinical records of all the leprosy patients enrolled in the Leprosy Clinic, during the years 1999–2019. The patient records fulfilling the diagnostic criteria of PNL were considered for analysis.

Results A total of 1225 patients registered leprosy cases, out of which 41 (3.3%) patients were diagnosed with PNL. Mean age was 31 years and 80% patients were male. Multiple nerves were affected in 25 (61%) patients and one nerve was found to be affected in only 16 (39%) patients. Grade 2 deformities were seen in 26 (63%) patients. All patients were treated with multi-drug therapy - 25 patients received the multibacillary regimen and 16 received the paucibacillary regimen; 27 (66%) patients completed the treatment as prescribed.

Conclusion Leprosy is the most common treatable cause of peripheral neuropathy. Therefore, early detection of leprosy neuropathy is important for preventing deformities and disabilities. It may be advisable to treat all PNL cases with the multibacillary multidrug therapy in view of higher rate of deformities.

Keywords: Leprosy, pure neural leprosy, *Mycobacterium leprae*, peripheral neuropathy, deformities

Introduction

Leprosy is a chronic infectious disease, caused by *Mycobacterium leprae*, which primarily targets the Schwann cells and involvement of skin occurs secondarily. Invasion of the nerve sheath by the bacilli induces inflammation and fibrosis, with consequent functional impairment and deformities.¹ Clinically, the skin lesions are the earliest and the most common presenting

Correspondence to: Dr. Mala Bhalla, Department of Dermatology, Venereology and Leprology, Government Medical College and Hospital, Sector-32, Chandigarh-160012, India (Tel.: +91-9646121545;

e-mail: malabhalla@yahoo.co.in)

[†] The two authors contributed equally to the manuscript and share first authorship.

feature due to their easy visibility, both cosmetically and socially. The various classifications and treatment regimens are also largely based on number and morphology of skin lesions.²

Pure neuritic leprosy (PNL) without cutaneous lesions was first recognized by Wade in 1952 and accepted as a subtype by the International congress at Madrid in 1953. The Indian Association of Leprologists (IAL) in 1955 recognized and included it in their six-group classification as 'Polyneuritic leprosy' and later renamed it as 'pure neuritic leprosy'.³ PNL is characterized by enlargement of peripheral nerves, sensory loss with or without motor loss in the absence of cutaneous lesions, slit skin smear (SSS) negativity and a variable lepromin test and histopathology.^{3,4} PNL exists as an entity with a considerable amount of ambiguity as researchers believe that it can be the initial presentation in 20% of leprosy cases and cutaneous lesions may develop in due course.³ There is a paucity of reports on this sub-type of leprosy. The prevalence of PNL varies from 4.3% to 5.6% in north India to 17.7% in south India.⁵ We share our experience of presentation, diagnosis, treatment and follow up of PNL patients from a tertiary care centre in North India.

Methods

In a retrospective analysis, the records of all the leprosy patients enrolled in the Leprosy Clinic at the Department of Dermatology, Government Medical College and Hospital, Chandigarh, India, during the years 1999–2019, were reviewed for clinically diagnosed PNL. Our hospital is an open access as well as tertiary care referral hospital in north India, catering to the population of Chandigarh and the patients from neighboring states, where leprosy is endemic. The diagnosis of PNL was confirmed and treatment was instituted. The patient records fulfilling the following diagnostic criteria of PNL were considered for analysis:

- (1) Peripheral nerve trunk or branch enlargement with sensory loss in its distribution with or without motor deficit not attributable to any other obvious cause.
- (2) No skin lesions.
- (3) SSS negative.

Relevant laboratory investigations such as slit skin smears (SSS) from one earlobe, one eyebrow and the area supplied by the involved nerve, skin biopsy and nerve biopsy wherever appropriate had been done in all patients as per clinic protocol. Other differential diagnoses of peripheral neuropathy including diabetes mellitus, hypothyroidism, Vitamin B12 and folate deficiencies, hereditary neuropathies, HIV-related distal symmetric polyneuropathy, chronic hepatitis B and C infection, alcoholism, toxin, drug and connective tissue diseases were excluded by detailed history and laboratory investigations wherever indicated. These included fasting blood glucose level, HbA1C, thyroid stimulating hormone level, vitamin B12 and folate levels, hepatitis B surface antigen, hepatitis C virus antibody and HIV ELISA and autoimmune profiles whenever required.⁶ All patients received WHO multi-drug therapy (MDT). Patients with 2 or more peripheral nerves involved received the multibacillary regimen (12 monthly packs of WHO-MB-MDT) and others with the paucibacillary regimen (6 monthly packs of WHO-PB-MDT). Patients with PNL were further classified according to the pattern of nerve involvement^{3,7,8}:

- (1) Mononeuritis - single nerve involvement.
- (2) Mononeuritis multiplex - asymmetric involvement of multiple nerves.
- (3) Polyneuritis - symmetric involvement of multiple nerves.

The study was approved by Institutional Ethics committee.

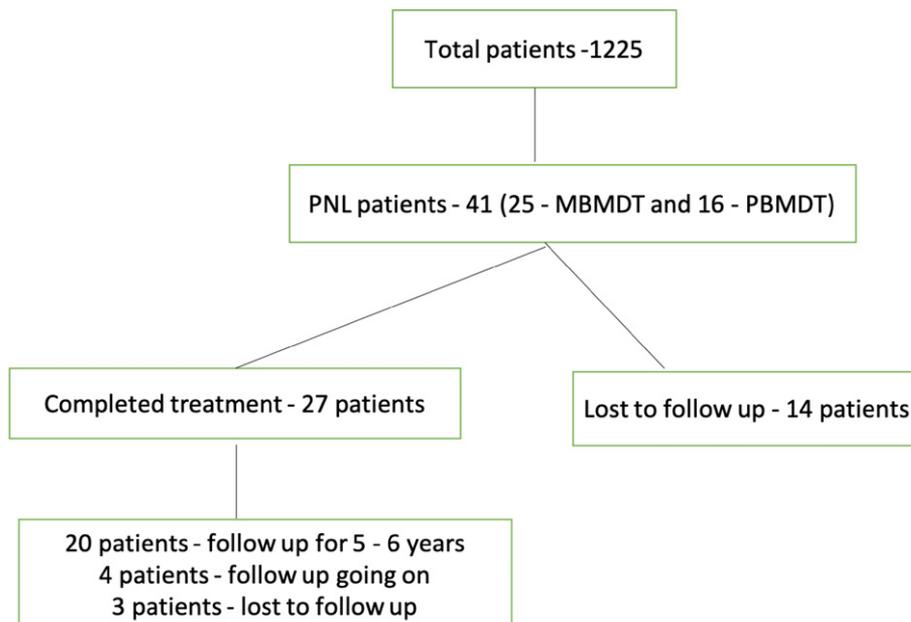


Figure 1. Flow chart depicting study participants. (PNL - Pure neuritic leprosy, MDT - multidrug therapy, MB - multibacillary, PB - paucibacillary.)

Results

A total of 1225 patients attended the leprosy clinic during the years 1999–2019, out of which 41 (3.3%) patients were diagnosed with PNL (Figure 1). Thirty-three (80%) patients were male and 8 (20%) were female with male: female ratio: 4.1:1. Mean age was 31 years (range 8–72 years) with 26/41 (63%) patients in the age group 15–35 years (Figure 2). Three (7%) patients were less than 14 years of age. About 95% patients were immigrants and 50% of them were from the highly endemic states of Uttar Pradesh (27%) and Bihar (24%) of India.

A history of smoking and alcoholism was present in 10 (24%) patients and no patient had any other associated co-morbidity. Six (15%) patients had a history of contact with leprosy patients, amongst which 3 (7%) had household contact. The earliest presentation was within 1 week and longest was 10 years, but most (56%) presented one year after the onset of symptoms. The most common symptoms with which patients presented were paraesthesia and sensory loss in the area supplied by the involved nerve.

Twenty-five (61%) patients had two or more nerves involved and one nerve was found to be affected in only 16 (39%) patients (Figure 3). Overall, upper limb nerves were more commonly affected than the lower limbs. Grade 2 deformities was seen in 26 (63%) patients presenting as claw hand in 20 (49%) and foot drop in 6 (14%) patients, while the remaining patients had grade 1 deformity only. Trophic ulcers, predominantly of the feet were seen in 9 (22%) patients.

The SSS was negative in all patients as per inclusion criteria. A nerve biopsy was performed in 5 patients and showed the specific histology of tuberculoid leprosy. Nerve biopsy could not be done in the other patients, either because no purely sensory nerve was involved or consent

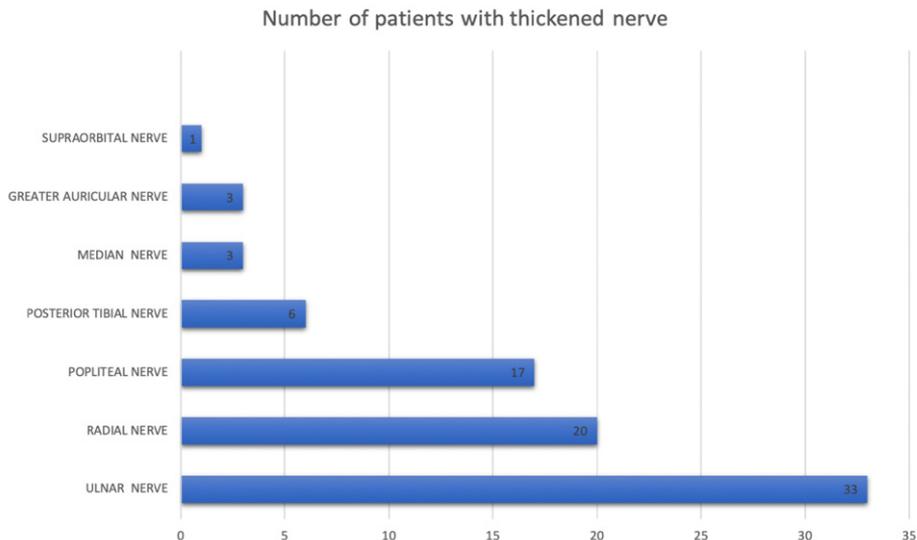


Figure 2. Number of patients with thickened nerves.

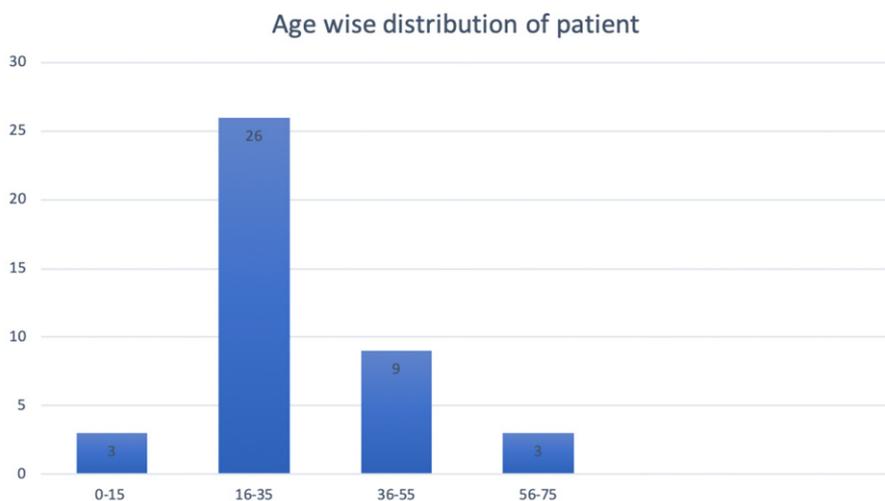


Figure 3. Age wise distribution of patients.

was refused. A skin biopsy was performed in 8 patients from a hypoaesthetic area, but showed normal epidermis and dermis.

All patients were treated with multi drug therapy (MDT) - 25 patients received the multibacillary regimen and 16 received the paucibacillary regimen. Of the total, 27/41 (66%) completed the treatment (amongst whom 20 patients received MBMDT and 7 received PBMDT) and responded well to the therapy. The remaining 14 patients were considered as defaulters because of incomplete treatment records and not being able to be traced through the contact information on record.

Four patients had type 1 reaction of whom two patients had features of acute neuritis at the time of presentation, one developed it while on treatment and one after one year of release from treatment. Features suggestive of type 1 reaction in PNL patients are - sudden increase in severity of neuritis, associated with increased nerve function impairment, recent loss of sensation in hands and feet, and loss of sweating, sensation, muscle strength in the area supplied by the nerve. All these four patients were treated with oral prednisolone (1 mg/kg/day in tapering doses) over 12 to 24 weeks. All patients were counseled about the need for follow up for a minimum period of 5 years and to report immediately in case of further skin lesions, new sensory or motor deficit or any other complaints. Among 27 patients who completed the treatment, 20 patients were followed up initially for a period of 2–3 years with regular outpatient visits and later contacted by telephone for a further 3 years. None of these patients developed any skin lesion during follow up. Follow up of 4 patients who presented in 2015–2017 is continuing and none has reported any skin lesions or new complaints. Three patients were lost to follow up after the completion of treatment.

Discussion

The proportion of PNL in the present study was 3.3% which is slightly lower than that reported in the literature.^{5,9–12} Males were predominantly affected in terms of prevalence and presence of deformities. Factors like repeated trauma of the anesthetic part due to increased exposure to outdoor occupations, labour work and greater mobility of this age group probably led males to be more vulnerable. In contrast to the majority of the previous studies^{9,13,14} in which most of the patients were aged above 40 years, the majority of our patients were in the 15–35 years group, which is consistent with the study conducted by Kumar *et al.*⁵ This could be due to early detection due to ongoing elimination campaigns or could be attributed to regional differences.

In the present study, mononeuritis multiplex was the most commonly observed pattern and this was consistent with previous studies,^{5,10–12} while a few studies reported mononeuritis as the most common pattern.^{9,13,15} Multiple mononeuropathy can be explained on the basis of undefined single route of infection which can be skin trauma or through the respiratory route, thus leading to involvement of more nerves in the latter case. Similar to other studies, the ulnar nerve was most commonly affected.^{5,10–12} This observation was in contrast to the study by Noordeen *et al.* where the lateral popliteal nerve was most commonly involved.¹³ Grade 2 disability was observed in 63% patients, equivalent to previously reported studies.^{10–12} The high rate of Grade 2 deformities in PNL patients is probably because of an effective immune response against *M. leprae* which helps in limiting the infection to the nerves and preventing dissemination, but leads to early and severe nerve damage, nerve paresis and consequent paralysis. Patients usually misinterpret the symptoms in the absence of skin lesions and initially consult with physicians or neurologists without any specific diagnosis. By the time these patients present to dermatologists, significant nerve damage has already occurred leading to deformities. Another factor contributing to the high rates of deformity in our patients could be referral bias as our hospital is a tertiary referral center where patients with severe manifestation are more likely to seek treatment.^{12,16}

Usually the diagnosis of PNL is based on clinical examination by palpation of nerves and by testing the sensory, motor and autonomic integrity along the area supplied by affected nerve. However, certain investigations such as nerve conduction studies, nerve biopsy, FNAC, qPCR have been shown to significantly aid the diagnosis in doubtful cases.⁴ Until now, there are no definite guidelines for diagnosis and management of PNL. Unlike the skin biopsy, nerve biopsy is an invasive and difficult procedure to carry out in each patient for the diagnosis and also a

purely sensory twig is not always available. As per definition in PNL, the SSS is negative and histopathology is not always available; so it is usually the number of nerve trunks involved that decides the choice of therapy between multibacillary or paucibacillary regimens.^{3,4}

Pure Neuritic Leprosy continues to be an enigma with most of the cases being reported from endemic countries. The variable clinical presentation, histopathology and lepromin status also plays its part in hindering the understanding of this entity. Some authors believe it to be the initial presentation of all types of leprosy, which gets recognized earlier in endemic areas because of raised awareness of the symptoms.³ As there is an effort to limit the disease to nerves in this entity, it should theoretically represent a paucibacillary form with a better immune response but this is not always true. Since none of the patients in the present study showed any skin lesions during their prolonged follow up, it lends support to the hypothesis that PNL is a separate entity rather than the initial presentation of the whole spectrum of leprosy patients. Newer techniques like electroneurography, serological and molecular diagnostic methods are becoming available and should be used for earlier detection of neural leprosy. This was also concluded in a study by Dos Santos DF where 78.6% patients received MBMDT because of *M. leprae* DNA positivity on SSS in clinical cases of PNL.⁷

Along with this, whether pure neuritic leprosy patients should be treated as PB or MB is still unclear. As SSS is negative in all patients according to the definition and a good immune response is mounted by the patients, these patients are treated as PB and MB according to the number of nerves involved, according to NLEP. But since the defaulting rate and rate of Grade 2 deformities is higher in such patients along with higher possibility of demonstration of *M. leprae* by newer diagnostic techniques, PNL may ideally be considered as a multibacillary form for treatment purposes. This is especially relevant in the present scenario where elimination of leprosy is the goal of all countries and it is better to overtreat these cases rather than undertreat them in view of higher rates of deformities which leads to more stigma. This is also probably the reason that the recent WHO guidelines have also proposed the same.

Limitation

- Lepromin test could not be performed.
- This present study was based on a retrospective analysis of hospital records, at a tertiary referral centre, so the reported prevalence rate might not reflect the actual burden of disease in general population.

Conclusion

Leprosy is the most common treatable cause of peripheral neuropathy. Therefore, early detection of leprosy neuropathy is important for preventing deformities and disabilities. Failure of early detection of leprosy often leads to severe disability and long-term morbidity, especially in cases of PNL where the clinical diagnosis usually gets delayed because of the relative absence of any defined diagnostic tests other than the clinical diagnosis. Newer serological and molecular techniques can be adopted for avoidance of misdiagnosis of patients and early treatment. It may be advisable to treat all PNL cases with the multibacillary multidrug therapy in view of higher rate of deformities.

Conflicts of interest

All authors declares no conflict of interest.

Source of funding

None.

References

- ¹ Scollard DM. The biology of nerve injury in leprosy. *Lepr Rev*, 2008; **79**: 242–253.
- ² Sehgal VN, Jain MK, Srivastava G. Evolution of the classification of leprosy. *Int J Dermatol*, 1989; **28**: 161–167.
- ³ Rao PN, Suneetha S. Pure neuritic leprosy: Current status and relevance. *Indian J Dermatol Venereol Leprol*, 2016; **82**: 252–261.
- ⁴ Jardim MR, Antunes SLG, Santos AR, Nascimento OJM, Nery JAC, Sales AM *et al*. Criteria for diagnosis of pure neural leprosy. *J Neurol*, 2003; **250**: 806–809.
- ⁵ Kumar B, Kaur I, Dogra S, Kumaran MS. Pure neuritic leprosy in India: an appraisal. *Int J Lepr Mycobact Dis Off Organ Int Lepr Assoc*, 2004; **72**: 284–290.
- ⁶ Trivedi S, Pandit A, Ganguly G, Das SK. Epidemiology of peripheral neuropathy: An Indian perspective. *Ann Indian Acad Neurol*, 2017; **20**: 173–184.
- ⁷ Santos DFD, Mendonca MR, Antunes DE, Sabino EFP, Pereira RC, Goulart LR *et al*. Revisiting primary neural leprosy: Clinical, serological, molecular, and neurophysiological aspects. *PLoS Negl Trop Dis*, 2017; **11**: e0006086.
- ⁸ Nascimento OJM. Leprosy neuropathy: clinical presentations. *Arq Neuropsiquiatr*, 2013; **71**: 661–666.
- ⁹ Mahajan PM, Jogaikar DG, Mehta JM. A study of pure neuritic leprosy: clinical experience. *Indian J Lepr*, 1996; **68**: 137–141.
- ¹⁰ Mendiratta V, Khan A, Jain A. Primary neuritic leprosy: a reappraisal at a tertiary care hospital. *Indian J Lepr*, 2006; **78**: 261–267.
- ¹¹ Kolleri JJ, Sasidharanpillai S, Vadakkayil B, Chathoth AT. A 10-year retrospective descriptive study on pure neuritic leprosy from a tertiary referral centre. *Indian Dermatol Online J*, 2019; **10**: 13–18.
- ¹² Narang T, Vinay K, Kumar S, Dogra S. A critical appraisal on pure neuritic leprosy from India after achieving WHO global target of leprosy elimination. *Lepr Rev*, 2016; **87**: 456–463.
- ¹³ Noordeen SK. Epidemiology of (Poly) neuritic type of leprosy. *Lepr India*, 1972; **44**: 90–96.
- ¹⁴ Pannikar VK, Arunthathi S, Chaccko CJ, Fritschi EP. A clinico-pathological study of primary neuritic leprosy. *Lepr India*, 1983; **55**: 212–221.
- ¹⁵ Pradhan S, Padhi T, Sirka CS, Nayak BP, Dash M. Clinico-epidemiological Profile of Pure Neuritic Hansen's Disease in Western Odisha: a Hospital Based Retrospective Cross Sectional Study. *Indian J Lepr*, 2018; **90**(4): 253–259.
- ¹⁶ Rathod SP, Jagati A, Chowdhary P. Disabilities in leprosy: an open, retrospective analyses of institutional records. *An Bras Dermatol*, 2020; **95**: 52–56.