



Nerve conduction study for early detection of leprosy

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Abstract

Background: Patient with wrist-drop and foot-drop was biopsied for mononeuritis multiplex. Diagnosis leprosy, came surprising as it was eliminated. Thus prompted, did research on electrophysiology data of leprosy patients referred for nerve conduction studies (NCS) Some mononeuritis multiplex patients diagnosed as vasculitis, became neuritic leprosy and biopsy results were incorporated.

Eliminated in 2005, leprosy is a public health challenge; due to high endemic areas with transmission, hidden cases, decreased case detection, administrative and political issues. Combining NCS with clinical examination detect cases & contacts early. NCS with nerve biopsy diagnoses pure neuritic leprosy before disability.

Objectives: (1) Use of NCS to study nerve involvement in leprosy. (2) Assess use of NCS & biopsy in pure neuritic leprosy

Study Design: Observational

Methods: Stored data-clinical & NCS of 36 patients and nerve-biopsy of seven pure neuritic leprosy-were collected from Electrophysiology records.

Results: Total 36 patients; abnormal NCS-34, nerve thickening-34. NCS was abnormal in 204 nerves; nerves thickened in 154. Six of 7 Neuritic & 11 of 29 others had disability. Disability risk is more for neuritic leprosy (RR-2.0714; CI- 1.2213-3.5133. p = 0.02).

Keywords: contacts, diagnosis, disability, leprosy, nerve-conduction-study, nerve-biopsy

Introduction

Leprosy causes disability and stigma by neurological deficits. Diagnosed clinically, by WHO (World Health Organisation) criteria of thickened nerves and anesthetic skin patches, it was declared eliminated, in 2005. Still leprosy is a public health challenge [1]. New cases, childhood and community cases are increasing leading to increasing disability and severity. This is due to presence of high endemic foci with ongoing propagation, clinically hidden cases and delayed diagnosis. Administrative factors like less skilled general health workers who are not so vigorous and impersistent in their work with disease occurrence in inaccessible locations [2] worsen the situation. Despite NLEP interference, situation is serious, in that in four Indian states, prevalence has crossed elimination point with more multibacillary cases and child rates over 10%. Administrative and political issues further complicate situation. Manpower for leprosy eradication were channeled as multipurpose workers for HIV/AIDS and tuberculosis, subsequently got integrated into general health care system. Siddiqui *et al.* pointed need for close monitoring for early diagnosis and prompt treatment. Health worker skills for diagnosis are decreasing, causing more time for definite diagnosis and treatment initiation. It causes contagious with occurrence of new cases leading to disability. General public is unaware of disease problem. All these resulted in reduced diagnostic skills and commitment of workers to leprosy eradication. Thus elimination process was literally arrested.

Hence more new cases, childhood cases and those with disabilities resulted [3]. Thus key issue is early diagnosis of contacts, women and children in high endemic areas, which will prove to be a major step towards eradication. Diagnosing neuritic leprosy, when early disability occurs, which is around [4] 50% is another problem. Pure neuritic leprosy occurs in 4.7-17% [5, 6]. Cranial nerves, peripheral nerves, sensory, motor and autonomic fibres are involved. Sympathetic involvement leads to dystrophic changes like fissuring, ulcer formation and mutilation. Early diagnosis reduces transmission and disability. Leprosy causing mononeuritis multiplex, polyneuropathy causing amputation and cranial neuropathy causing blindness, which is a preventable and treatable neuropathy.

NCS detects NFI (Nerve Function Impairment) earlier before clinical signs manifest [7]. Disability and deformity could be minimised if nerve function impairment (NFI) is detected and treated early. NFI is clinically 33-56%, with NCS, it is over 80-98% [8].

Though usefulness of NCS was reported in 1990⁸, NCS was not used commonly. Availability of modern, affordable, portable Electrophysiology machines with trained technicians, less time will be consumed for each study. Use of tele-medicine for reporting NCS findings and using single machine, many cases and contacts could undergo combined clinical examination and screening NCS in the field in high endemic areas.

Sensory NCS of common peripheral nerves are useful for early detection of nerve damage^[8]. NCS is objective, assesses severity and localises maximum involvement^[9]. Common sensory and motor NCS requires less expertise; with sensory, it is reduced conduction velocity and in motor nerves it is amplitude of action potential (CMAP) or both, depending if it is demyelinating or axonal. NCS is safe and common^[9].

From electrophysiology laboratory under Neurology Department, Government Medical College, Kottayam, retrospectively patients' data-clinical, NCS and nerve biopsy were collected. Patients were referred from Neurology and Dermatology OPDs of Govt. Medical College, Kottayam. Nerve biopsy was conducted in Pathology Department, Govt. Medical College, Kottayam.

This study looked into severity and type of nerve involvement in leprosy. Which identifies NFI (nerve function impairment) early and better- clinical exam or NCS or combination of both. Detection of pure neuritic leprosy is important due to increasing atypical forms^[10] Technician expertise and physician awareness in Leprosy detection are decreasing^[11]. Nerve biopsy is useful in diagnosing pure neuritic leprosy^[12] is reported from 1988. High index of suspicion, physical examination and NCS will detect Leprosy before disabilities.

Objectives

1. Use of NCS to study nerve involvement in leprosy
2. Assess use of NCS & biopsy in pure neuritic leprosy

Study Design

Retrospective, Observational study from acquired clinical, electrophysiology and nerve biopsy data

Sample Size

All confirmed leprosy patients referred for NCS in the stipulated period was included.

Study Setting

Electrophysiology laboratory, Dept. of Neurology, Govt. Medical College, Kottayam

Materials and Methods

Confirmed, leprosy patients, referred from Out Patient Departments of Neurology and Dermatology, Government Medical College, Kottayam, Kerala, underwent NCS, both sensory and motor of upper and lower limbs. Nerve biopsy results of pure neuritic leprosy patients were collected. Nerve biopsy was done at Department of Pathology, Government Medical College, Kottayam, Kerala. Study period was from Jan 2015 to Jan 2017. Data was collected from stored records.

Inclusion Criteria

All leprosy patients referred to electrophysiology laboratory during study period.

Exclusion criteria

Peripheral nerve diseases, radicular diseases and anterior horn cell diseases were excluded History and Physical examination findings including nerve thickening and skin lesions were noted Disability grading by W.H.O grading system^[13, 14] was also noted.

Data of NCS-motor & sensory studies of peripheral nerves- median, ulnar, common peroneal and posterior tibial nerves and sensory studies of radial, ulnar cutaneous and sural nerves were collected. Parameters were distal latency, amplitude, conduction velocity of compound muscle action potential (CMAP) and sensory nerve action potential (SNAP). Normal adult values were used for comparison^[15].

Nerve biopsy results of pure neuritic leprosy were incorporated.

Statistical Analysis

Statistically neuritic form is having high risk for developing disability. (RR-2.0714; CI- 1.2213-3.5133. p = 0.02)

{epi-info. cdc. Atlanta}. Was done by epi-info cdc Atlanta.

Observations

Thirty-six cases of leprosy were included. Youngest was 5 years and oldest 69 years; 27 were males and 9 females. Two subjects who did not have nerve thickening had abnormalities in nerve conduction of two nerves each and two patients, with normal nerve conduction, each had two nerves thickened.

Common nerves affected were ulnar and radial cutaneous nerve. 204 nerves were affected electro physiologically as compared to 154 thickened ones, majority (32/36) were mono neuropathy multiplex.

Among pure neuritic forms (TABLE-1); No-3 and 4 had single nerve thickening, while others had multiple nerves affected but by NCS many more were affected; all had mono neuritis multiplex. Definitive diagnosis was from nerve biopsy. Six had disability; four grade two, two grade one.

Two patients (patient no. 4 & 6 of TABLE-2), had no nerve thickening, classified as paucibacillary should be classified as multibacillary (if nerve involvement occurred irrespective of it being found by clinical exam or NCS). So is case with 2 and 10. NCS revealing more abnormality (two more nerves affected). Two of 36 (patient no.3 &5 of table-2) had normal NCS, presented with thickening of two nerves.

Twenty-nine patients had multiple nerve thickening, five had single nerve thickening; majority had mono neuritis multiplex and poly neuropathy for two by NCS. All patients had nerve involvement of more than one nerves, categorising them into multibacillary, when both NCS and nerve thickening were considered.

Eleven of 29 patients with skin lesions and with/without neurological symptoms (excluding pure neuritic type) had disability (38%); grade 2 for 5 (17%) and grade 1 for 6(20%) Among pure neuritic form, 6 had disability (6/7); four had grade 2 disability and two had grade 1(85% disability for neuritic). Statistically neuritic form is having high risk for developing disability. (RR-2.0714; CI- 1.2213-3.5133. p = 0.02){epi-info. cdc. Atlanta}. Nerve biopsy in pure neuritic form showed granuloma, giant cells and macrophages and one, showed foam cells.

Discussion

Nerve thickening was seen clinically in 34 of 36 patients, total of 154 nerves. NCS showed abnormality in 34 patients, but number of nerves affected were 204. It revealed more and severe involvement than clinical examination, helping in categorising for treatment optimisation, duration and drug

selection. Usefulness of NCS in leprosy was reported in 1970s, where clinically normal nerves showed conduction abnormality. Ramadan showed clinically up to 80% nerves showing conduction abnormalities [16, 17] thickened nerves can have normal conduction parameters, latter seen in present study also. Two patients with (No 4 & 6 of table-2) skin lesions had abnormal nerve conduction in three nerves; showing clinically normal nerves can be electro physiologically abnormal due to preclinical disease. They will manifest neurological symptoms on follow up [18].

Two patients had normal NCS, presented with thickened nerves. Clinically thickened nerves could have normal conduction parameters [18] Normal NCS could be due to damage confined to few nerve fibres, faster and more number of fibres escaping abnormality [18].

Nerve involvement was seen in all patients either by NCS or by clinical examination. This is in contrast to 20% involvement, but later studies have shown to be having up to 80% nerve involvement which were clinically silent [18, 19]. NCS in combination with clinical examination is useful in identifying and grading leprosy, giving early and complete treatment making patients disability-free due to disease or treatment [18].

Six patients were pure neuritic; accounting for 17% of total. All had abnormal nerve conduction parameters. Five of them had histo pathological findings of leprosy. In India, reported incidence of pure neuritic Hansen's disease was 17.7% and 4.2% [5, 6]. Incidence is higher in South India. Following declaration of elimination of leprosy in 2005, atypical forms are increased [1, 10]. Of pure neuritic presentation in 7 patients, six had disability. Two had grade 1 and three had grade 2. About 50% of neuritic had grade 2 disability and overall 80% had disability. Kaur had found 31.5% deformities and Mahajan 48.6% [20].

Disability should be detected early. If Grade 1 disability is treated early, deformity could be prevented, as disability occurs due to nerve involvement by different mechanism of action like trauma from sensory loss, autonomic dysfunction and immunological reaction [21]. NCS can be used as complimentary investigation along with clinical examination [18].

Though elimination of leprosy was achieved, even now it continues to form an important cause of neuropathy and disability in India [22, 23]. Diagnostic delay is significant causing disability and concern in patients and health care workers [24] Monalisa *et al.* looked into histopathology of nerve biopsy specimens for two years referred for unexplained neuropathy; 60 biopsies were leprosy, 46 pure neuritic; mononeuritis multiplex formed majority but there were poly

neuropathy and mono neuropathy [26]. This study shows significance of pursuing neuropathy, arriving at definite diagnosis with NCS and nerve biopsy in detecting treatable neuropathies (Leprosy).

High index of suspicion should be exercised when patient presents with neurological symptoms of tingling, numbness, sensory loss with painful and thickened nerves and referred for NCS when early nerve biopsy could be done.

In 26/36 patients, presence and severity of nerve involvement could be assessed by NCS than by examination. Thus NCS is sensitive than clinical examination. But, all patients were detected to have neuritis when both are combined

In subjects with skin and nerve involvement, clinical examination for skin lesions, nerve thickening, NCS of motor and sensory nerves identified all cases. But in two cases presenting as skin lesion alone, NCS yielded positive result. Thus 9 of 36 (pure neuritic-7 and with skin lesions only-2) patients required NCS and nerve biopsy to arrive at diagnosis of Hansen's disease. Leprosy is primarily disease of nerves and disability with stigma is due to nerve involvement. With multidrug therapy, incidence of infective forms had come down in certain areas, atypical forms like single lesion, organ involvement¹ and pure neuritic forms are seen. In those cases, nerve biopsy is more informative and specific in diagnosis when other investigations are inconclusive [25].

Four of 7 neuritic patients developed grade 2 disability and two patients developed grade 1 disability in a year. Hence early detection by NCS and nerve biopsy in undiagnosed peripheral neuropathy where there is high index of suspicion is emphasized [25].

Reason for disability is delay in diagnosis and treatment initiation [24]. In addition, after declaration of 'Eradication of leprosy', sensitization and exposure of health care professional to atypical and rare forms of leprosy is less which delays early diagnosis [3, 24] In addition, to prevent nerve involvement and its consequences early detection and periodic evaluation by nerve conduction study should be emphasised in worsening neurological status to initiate steroids and other immunomodulation agents [18].

Study by Monalisa *et al* and present one, all cases of unexplained poly neuropathy or mono neuritis multiplex should be subjected to early NCS with nerve biopsy²⁵, as leprosy neuritis is amenable to early treatment and prone for disability. Present study emphasizes need to shift diagnosis of leprosy from pure clinical examination to clinical and NCS of common peripheral nerves even in field scenario to increase detection in asymptomatic contacts. Diagnosis of leprosy requires more expertise than it used to be earlier in the present state of affairs.

Table 1: Clinical, NCS and nerve biopsy details of patients with pure neuritic leprosy

S. No.	age	Sex	Duration	Disability	Nerves thickened	NCS-sensory	NCS-motor	Slit skin smear	Nerve Biopsy	PB/MB	Reaction
1	40	M	<1yr	1	2	2	2	-	+	MB	-
2	47	M	>1yr	2	3	2	2	-	+	MB	-
3	59	M	>1yr	2	1	3	2	-	+	PB	-
4	36	M	>1yr	2	1	3	3	-	+	MB	-
5	55	F	<1yr	1	3	6	2	-	+	MB	-
6	34	M	<1yr	0	3	2	1	-	+	MB	-
7	45	M	>1yr	2	9	9	9	-	+	MB	-

NCS-Nerve conduction study; PB-Paucibacillary; MB-Multibacillary

Among 7 pure neuritic form-(TABLE-1); 3 and 4 had single nerve thickening, while others had multiple nerves affected but by NCS many more were affected; all had mono neuritis

multiplex. Definitive diagnosis was from nerve biopsy. Six had disability; four grade two, two grade one.

Table 2: Clinical and NCS details of patients without neurological symptoms

S. no	age	Sex	duration	Dis ability	Thick nerves	NCS Sensory-no. affected	NCS Motor- no. affected	Slit skin smear	PB/ MB	React ion
1	69	M	<1	0	5	5	3	-	MB	-
2#	58	M	<1	0	1	Normal	2	-	PB	+
3	5	M	<1	0	2	Normal	Normal	-	PB	-
4#	38	F	<1	0	Nil	3	Normal	-	PB	-
5	19	M	<1	0	2	Normal	Normal	-	MB	-
6#	16	M	<1	0	Nil	2	1	-	PB	-
7	25	M	<1	1	3	2	2	-	MB	-
8	46	M	<1	0	3	2	2	-	MB	-
9	24	M	<1	0	2	2	1	-	MB	-
10#	32	F	>1	0	1	2	2	-	PB	+
11	35	M	<1	0	4	3	Normal	-	MB	-
12	38	F	>1	1	1	6	2	-	MB	-
13	44	F	<1	1	3	3	4	+	MB	-
14	45	F	>1	0	4	2	4	+	MB	-
15	46	M	>1	0	3	1	3	-	MB	-

Two patients (patient no. 4#&6# of TABLE-2), did not have nerve thickening and classified as paucibacillary could be classified as multibacillary (if nerve involvement occurred irrespective of it being found by clinical exam or NCS). So is

case with#2 and #10. NCS revealing more abnormality (two more nerves affected). Two of 36 (patient no.3 &5 of table-2) had normal NCS, presented with thickening of two nerves.

Table 3: Clinical and NCS details of patients with lesions and nerve involvement

S. No.	age	sex	duration	disability	Thick nerves	NCS-sensory	NCS-motor	Slit skin smear Exam	PB/MB	Reaction
1	30	M	<1	2	4	1	1	+	MB	-
2	49	F	<1	0	2	3	5	+	MB	-
2	49	F	<1	0	2	3	5	+	MB	-
3	47	M	>1	2	5	4	4	+	MB	-
4	47	M	<1	1	1	2	2	+	MB	-
5	43	M	<1	1	5	3	3	+	MB	-
6	49	M	<1	1	6	2	2	+	MB	+
7	22	M	<1	0	8	5	5	+	MB	+
8	68	M	<1	2	12	All nerves involved	All nerves involved	+	MB	-
9	40	F	>1	2	12	7	7	+	MB	-
10	16	M	<1	0	4	3	3	-	MB	-
11	26	M	<1	0	4	2	2	-	MB	-
12	36	M	<1	0	4	4	4	-	MB	-
13	34	M	<1	2	5	3	3	-	MB	-
14	35	M	<1	0	2	2	2	+	MB	+

Table-3 showing all having multi-bacillary leprosy, showing both skin and nerve involvement

Conclusion

Pragmatists, working at peripheral centres, do minimal investigations, miss rare diseases, completists at referrals, extensively investigate. In leprosy it is wise to combine essential investigations for best results, eradication.

Nerve involvement is seen in all cases of leprosy. NCS is needed for early diagnosis and thus optimal management of all types of leprosy

In clinically suspected cases of peripheral neuropathy as pure neuritic Leprosy, NCS with nerve biopsy is recommended to know extent and type of nerve involvement and early treatment to prevent disabilities.

In all cases of unexplained poly neuropathy, mono neuropathy or mono neuritis multiplex, nerve biopsy is strongly recommended to rule out diagnosis of Leprosy.

Message

Clinical examination in fields will miss early diagnosis in contacts and house-holds, hindering eradication process. As nerve involvement is seen in all leprosy types, NCS of common nerves has to be part of field activities to increase detection rates, pure neuritic forms and for early treatment initiation for reducing contagious and disability.

Limitations

Small Numbers

Kottayam is district with high literacy in Kerala and good

socio-economic status. Hence numbers were small.

Strengths

There was a child of 5yrs. All patients included had nerve involvement which strengthens study and need for combined approach.

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