

Original Research Article

Prospective study on usefulness of sural-nerve biopsy

Nipun Sapru¹, Roma Singh^{2*}

¹Department of Neurology, Government Medical College and Super-Specialty Hospital Jammu, Jammu and Kashmir, India

²Consultant Pathologist, Jammu, Jammu and Kashmir, India

Received: 08 August 2021

Accepted: 08 September 2021

*Correspondence:

Dr. Roma Singh,

E-mail: romasingh14689@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Peripheral neuropathies are a heterogeneous group of disorders, but common among patients attending neurology clinics. A systematic approach, like sural nerve biopsy, is the need of the hour, for a cost effective diagnosis. Studies have shown that nerve biopsy improves treatment in up-to 60% patients. Present study was conducted to evaluate the clinical profile and usefulness of sural nerve biopsy in peripheral neuropathy.

Methods: A prospective study was conducted in the Department of Neurology in collaboration with Department of Pathology, Medanta: The Medicity, Gurugram, for a period of six months from January 2019- June 2019. Out of total 82 randomly selected patients, 43 patients were selected for nerve biopsy.

Results: Mean age in the biopsy group was 45.61±19.24 years. Duration of illness was less than 1 year in 60.5% patients. In 39.5% of cases, nerve biopsies established the diagnosis and in total 77% of cases it was worthwhile. Hansen's disease was diagnosed in 44%, CIDP in 12%, Vasculitis in 14%, and diabetes in 7% patients. Biopsy proved more diagnostic when tingling and numbness was there. Diminished DTRs was also statistically significant symptom in biopsy favoring group. Nerve biopsy in multiple mononeuropathy (65.1%) proved more beneficial than in polyneuropathy (32.6%). Similarly, motor-sensory was a predominant presentation in 28 (65.1%) patients with nerve biopsy being more valuable.

Conclusions: Nerve biopsy, having a good diagnostic yield, can be a useful aid in cases with multiple mononeuropathy. It can be the key to prevent long term neurological complications in patients.

Keywords: Nerve biopsy, Peripheral neuropathy, Sural nerve

INTRODUCTION

Peripheral neuropathies are amongst the most common disorders among patients attending neurology clinics. Nerve biopsy has been found essential in establishing etiological diagnosis of peripheral neuropathy, especially in cases of vasculitis, leprosy, etc.¹ Several factors determine the diagnostic utility of nerve biopsy, the most important being the pre-biopsy diagnosis. A step-wise systematic approach comprising a good clinical history, a thorough neurological and systemic examination, electro diagnostic studies and relevant biochemical tests should be therefore be undertaken in all cases.

Studies have shown that nerve biopsy improves treatment in an estimated 60% of patients.^{2,3} However, in only 20% of patients of vasculitis, in whom biopsies were performed, sural nerve biopsy could yield unequivocal evidence.⁴ A biopsy of the superficial peroneal nerve combined with a peroneus brevis muscle biopsy could confirm a higher yield, possibly due to higher frequency of involvement of the peroneal nerve in vasculitic neuropathy and the frequent involvement of muscle arteries.⁵ Present study was conducted on patients attending the neurology outpatient department, or admitted in the wards, to evaluate the clinical profile and usefulness of sural nerve biopsy.

METHODS

A prospective randomized observational study was carried out in the Department of Neurology in collaboration with Department of Pathology, Medanta: The Medicity, Gurugram, for a period of six months from January 2019-June 2019. The study was conducted on randomly selected 82 patients suffering from peripheral neuropathy. Proper written consent was obtained from all participants. The neuropathy was considered disabling when sensorimotor deficit of peripheral origin leads to impairment of activity of daily living. Patients suffering from a disabling neuropathy of known origin were included in the study only when uncommon manifestations were present.

All patients had routine blood tests, biochemical assays and protein electrophoresis. Neurological interview and examination was carried out in a standardized manner. Number and distribution of affected nerves were recorded. Nerve thickening was ascertained. Sensory impairment, motor deficit, and deformity status were assessed. The distribution of motor and sensory symptoms were recorded as distal symmetrical, distal asymmetrical, or focal or multifocal. A family history of neurological disease was also recorded.

In cases of symmetrical neuropathies one upper limb and one lower limb were evaluated while in asymmetrical neuropathies at least three limbs were evaluated. Tibial, common peroneal and sural nerves were evaluated in the lower limbs. Variable like: distal motor latency, motor and sensory conduction velocity, the amplitude of the compound muscle action potential, F wave and sensory nerve action potential, were measured and considered abnormal only when they exceeded the limits of normality by 2 SDs. Sural nerve biopsy was carried out in those patients in whom the clinical, electro diagnostic, and the biochemical tests were found inconclusive. Sural nerve biopsy was carried out as per the standard procedure, under aseptic precautions.

Gluteraldehyde/formalin fixed nerve biopsies were processed for paraffin embedding and sectioned in transverse and longitudinal planes. Four-6 micron thick sections were routinely stained with hematoxylin-eosin (HE) for morphological examination and masson's trichrome (MAT) for collagen. For the Kultshitsky-pal (K-pal) stain for myelin, a small segment of fixed nerve was placed overnight in Fleming's solution and processed the next day for paraffin embedding. Final diagnosis was made after biopsy. If diagnosis was not evident then cryptogenic neuropathy was labeled.

To evaluate the yield of nerve biopsies, we referred to the criteria published by Midroni et al and Argov et al.^{6,7} Diagnostic showed abnormalities specific or highly

suggestive of a definitive diagnosis. Contributory provided information that was either essential or helpful for the patient's management. Non-contributory did not influence patient's management and was not revealed any significant information helping in diagnosis or management of patient.

The data was analysed using MS Excel 2010 software and significant difference between proportions was tested by Fishers's exact probability test.

RESULTS

Out of total 82 patients, 43 patients were selected for nerve biopsy and the rest 39 patients, were diagnosed using routine investigations and detailed clinical electrophysiological examinations. Age ranged from 14 to 70 Years, with the mean age in biopsy group patients was 45.61 ± 19.24 years. Maximum patients being in the age groups: above 60 years (34.9%) and below 30 years (25.6%). Male to female ratio was: 28:15 (1.87:1). Total duration of illness before biopsy varied from 1 month to 16 years, however, maximum number of patients (60.5%) had duration of illness less than 1 year (Table 1).

Table 1: General demographic profile of patients.

		Nerve-biopsy group		Non-biopsy group	
Characteristics		Number	%	Number	%
Age (years)	Below 30	11	25.6	12	30.8
	30 to 45	8	18.6	7	17.9
	46 to 60	9	20.9	9	23.1
	Above 60	15	34.9	11	28.2
Gender	Males	28	65.1	24	61.5
	Females	15	34.9	15	38.5
Duration of illness	<1 year	26	60.5	20	51.3
	>1 year	17	39.5	19	48.7

Multiple mononeuropathy was present in 65.1% and polyneuropathy was found in 32.6%. Motor-sensory was most predominant sensory presentation in 28 (65.1%) patients, however, in 50% (14) patients it was contributory only. Weakness was present in 38 (88.4%) of patients, which was asymmetrical in 60.5% (26) patients (Table 2).

In 17 cases the nerve biopsy had changed the preferred diagnosis or gave diagnosis otherwise even not suspected. This group was called as 'diagnostic'. In 16 cases the biopsy had contributed by confirming a diagnosis which had already been suspected. This group was called as 'contributory'. In 10 cases the biopsy did not contribute to the diagnosis and thus those patients remained undiagnosed and were called as 'idiopathic' with the nerve biopsy being 'noncontributory' (Tables 2 and 3).

Table 2: Clinical and electrophysiological profile of nerve-biopsy patients.

	Diagnostic	Contributory	Non-contributory	Total (%)	P value
Total number of patients	17	16	10	43 (100)	--
Clinical presentation					
Multiple mono-neuropathy	13	13	2	28 (65.1)	<0.05*
Poly-neuropathy	5	3	6	14 (32.6)	
Impaired JP/vibration	10	10	4	24 (55.8)	
Diminished DTRS	11	6	3	20 (46.5)	<0.05*
Tingling	16	13	4	33 (76.7)	<0.05*
Numbness	15	12	6	33 (76.7)	<0.05*
Sensory motor involvements					
Sensory	8	2	5	15 (34.9)	<0.05*
Motor-sensory	11	14	3	28 (65.1)	
Electrophysiological study findings					
Axonal	15	12	7	34 (79.1)	
Demyelinating	5	3	1	9 (20.9)	

*p<0.05 = significant

Diagnosis was Hansen's disease in 44%, CIDP in 12%, vasculitis in 14%, and diabetes in 7% patients. Final diagnosis could be made in only 77% of patients, while 23% remained undiagnosed (Table 3).

Table 3: Final diagnosis in nerve-biopsy group.

Final diagnosis	No. of patients (%)
Hansen's disease (HD)	19 (44)
Chronic inflammatory demyelinating neuropathy (CIDP)	5 (12)
Vasculitis	6 (14)
Diabetic	3 (7)
Undiagnosed	10 (23)
Total	43 (100)

Out of 19 leprosy (Hansen's disease) patients nerve biopsy revealed epithelioid granuloma in 8 patients and inflammatory infiltrate in 14 patients. Biopsy was found to be more helpful in multiple mono-neuropathy patients than in polyneuropathy. Similarly patients with mixed presentation were more likely to diagnosed by nerve biopsy than with predominant sensory complaints. Diminished DTRs, tingling and numbness were statistically significant in biopsy favoring groups than in non-contributory group.

DISCUSSION

With hereditary neuropathies, it is now seldom necessary to perform a morphological study of a nerve biopsy specimen. In multifocal neuropathy, nerve biopsy more often contributes to the diagnosis than in the other patterns of neuropathy.⁸ In the current study, the treatable cases which remained undiagnosed/inconclusive after clinical, electro diagnostic and biochemical evaluation were mainly considered. Only 43 out of 82 consecutively

reporting patients (selected randomly) underwent sural nerve biopsy for a disabling neuropathy, as in the other 39 patients, the detailed clinical history and meticulous neurological examination with first line routine investigation, proved to be sufficient.

Neundorfer et al in 1990, considered that the biopsy was "crucial" for establishment of the diagnosis in 27% of patients and confirmed a previously suspected diagnosis in 37%.⁹ Our results were quite in line to this as they showed that in 17 (39.5%) patients, nerve biopsies established the diagnosis, while in 16 (37.2%) cases patients nerve biopsy proved to be contributory, helping in confirming diagnosis or in excluding other causes of neuropathy. In total, in about 33 (77%) of cases, performing nerve biopsy proved to be worthwhile and in 10 patients, the biopsy did not contribute to the diagnosis and they remained undiagnosed and were called as 'idiopathic' with the nerve biopsy being 'noncontributory'. Similar to this, a prospective study by Gabriel et al found that 84% patients got advantage from nerve biopsy.² Oh et al also reported helpful results in 45% biopsies.¹⁰ In a retrospective study of by Hughes et al they also noted a change in diagnosis in 17% of 36 patients.¹¹

In this study leprosy neuropathy (44%) was found most common cause of undiagnosed peripheral neuropathy, which indicates that leprosy is still most common cause of treatable peripheral neuropathy in Indian towns and villages reporting incidence in the range of 5.5% to 17.7% of all leprosy cases.¹² Leprosy neuropathy almost always occurs in conjunction with a certain type of skin lesion. The presence of nerve deficit in patients from endemic areas who did not have skin lesions is considered sufficient reason for a pure neural leprosy (PNL) diagnosis.^{13,14} Vasculitic neuropathy, on the other hand, was demonstrated in 6 patients through biopsy and was found very likely in 5 more patients, accounting for a

total of 11 (25%) of the cases. In a study by Chia et al on patients over the age of 65 years with disabling neuropathy, more than one third had a vasculitic neuropathy, and 25% had either CIDP or dysglobulinaemic neuropathy.¹⁵ Other such studies were supporting these finding too.¹⁶⁻¹⁷

A correlation between the clinical and electrodiagnostic findings with the nerve biopsy revealed that impaired joint position and vibration was more in group of patients in which biopsy proved useful, besides, a significant correlation was found in presence or absence of tingling and numbness. Biopsy proved more diagnostic and statistically significant when tingling and numbness was there than absence of it. Diminished DTRs was also statistically significant in biopsy favoring group than in non-contributory group.

In patients with the clinical pattern of multiple mononeuropathy, nerve biopsy proved more beneficial than polyneuropathy group ($p < 0.05$). Similarly in patients with sensorimotor symptoms nerve biopsy was more significant and valuable.

The limitation of this study lies is that it was conducted on mixed population being tended by a reputable tertiary health care centre and hence the results cannot be generalized on the local populace or population of any given geographical area around it.

CONCLUSION

Nerve biopsy, having a good diagnostic yield, can be a useful aid in neuropathy patient management. It is especially useful in cases with multiple mononeuropathy. In context of Indian population, facing endemic of leprosy and vasculitis diseases, keeping a high index of suspicion, taking an early start and careful selection of patient group for nerve biopsy, can be the key to prevent long term neurological complications in patients. More such studies are needed to be conducted among multi-centric and larger populations for arriving at more precise data on the subject.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

- Patidar SP, Joshi D, Mishra VN, Chaurasia RN, Ansari AZ. Diagnostic yield of sural nerve biopsy: study from a tertiary care referral centre in India. *J Neurol Neurosci*. 2016;6:1.
- Gabriel CM, Howard R, Kinsella N, Lucas S, McColl I, Saldanha G, et al. Prospective study of the usefulness of sural nerve biopsy. *J Neurol Neurosurg Psychiatr*. 2000;69:442-6.
- Argov Z, Steiner I, Soffer D. The yield of sural nerve biopsy in the evaluation of peripheral neuropathies. *Acta Neurol Scand*. 1989;79:243-5.
- Hellmann DB, Laing TJ, Petri M, Whiting-O'Keefe Q, Parry GJ. Mononeuritis multiplex: the yield of evaluations for occult rheumatic diseases. *Medicine (Baltimore)*. 1988;67:145-53.
- Said G, Lacroix-Ciaudo C, Fujimura H, Blas C, Faux N. The peripheral neuropathy of necrotizing arteritis: a clinicopathological study. *Ann Neurol*. 1988;23:461-5.
- Midroni G, Bilbao JM. Examination of the peripheral nerve biopsy. In: Midroni G, Bilbao JM, eds. *Biopsy diagnosis in peripheral neuropathy*. Newark, Butterworths; 1995;241-262.
- Argov Z, Soffer D, Steiner I. The yield of sural nerve biopsy in the evaluation of peripheral neuropathies. *Acta Neurol Scand*. 1989;79:243-5.
- Said G. Indications and usefulness of nerve biopsy. *Arch Neurol*. 2002;59(10):1532-5.
- Neundörfer B, Grahmann F, Engelhardt A, Harte U. Postoperative effects and value of sural nerve biopsies: a retrospective study. *Eur Neurol*. 1990;30:350-2.
- Oh SJ. Diagnostic usefulness and limitations of the sural nerve biopsy. *Yonsei Med J*. 1990;31:1-26.
- Hughes RA, Adams CW, Hall S. The contribution of nerve biopsy to the management of peripheral nerve disease. *J Neurol Neurosurg Psychiatr*. 1990;53:714.
- Talwar S, Jha PK, Tiwari VD. Neuritic leprosy: epidemiology and therapeutic responsiveness. *Lepr Rev*. 1992;63:263-8.
- Mahajan PM, Jogaikar DG, Mehta JM. A study of pure neuritic leprosy: clinical experience. *Indian J Lepr*. 1996;68:137-41.
- Uplekar MW, Antia NH. Clinical and histopathological observations on pure neuritic leprosy. *Indian J Lepr*. 1986;58:513-21.
- Chia L, Fernandez A, Lacroix C, Adams D, Planté V, Said G. Contribution of nerve biopsy findings to the diagnosis of disabling neuropathy in the elderly. A retrospective review of 100 consecutive patients. *Brain*. 1996;119:1091-98.
- Barach JK. Peripheral neuropathy (PN) in elderly population (65 years and above). *Neurology*. 1989;39:208.
- Huang CY. Peripheral neuropathy in the elderly: a clinical and electrophysiologic study. *J Am Geriatr Soc*. 1981;29:49-54.

Cite this article as: Saprou N, Singh R. Prospective study on usefulness of sural-nerve biopsy. *Int J Res Med Sci* 2021;9:3095-8.