Clinical Neurophysiology 127 (2016) 2747–2755

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Comprehensive electrophysiology in leprous neuropathy – Is there a clinico-electrophysiological dissociation?

Neeraj Kumar [a,1], Hardeep Singh Malhotra [a,*], Ravindra Kumar Garg [a,2], Rakesh Lalla [b,3], Kiran Preet Malhotra [c,4], Amita Jain [d,5], Imran Rizvi [a,6]

[a] Department of Neurology, King George's Medical University, U.P., Lucknow 226003, India
[b] Breach Candy Hospital, Mumbai, India
[c] Department of Pathology, R.M.L. Institute of Medical Sciences, Lucknow 226010, India
[d] Department of Microbiology, King George's Medical University, U.P., Lucknow 226003, India

ARTICLE INFO

Article history:
Accepted 2 May 2016
Available online 17 May 2016

Keywords:
Leprosy
Neuropathy
Great auricular nerve
Sympathetic skin response
Mononeuritis multiplex

HIGHLIGHTS

- Electrophysiological dissociation is common in patients with leprous neuropathy.
- Nerve thickening may neither correspond nor predict electrophysiological deficits.
- Combination of thickened great auricular, ulnar and common peroneal nerves suggests leprous neuropathy.

ABSTRACT

Objective: The diagnosis of leprous neuropathy is mostly empirical and electrophysiological studies may not truly represent the clinical findings. This study comprehensively evaluates the neuroelectrophysiology and looks at clinico-electrophysiological dissociation.
Methods: Conventional electrophysiological recording included evaluation of median, ulnar, radial, tibial, and common peroneal nerve; an extended protocol included great auricular, phrenic, and facial nerves, along with sympathetic skin response and blink reflex. Nerve biopsy and slit skin smear were done to aid categorization.
Results: Forty-six patients of leprosy were enrolled. Mononeuritis multiplex was the commonest presentation. Sensory loss was commoner than motor deficits. Approximately 60% of all cases were nerve-biopsy proven. Nerve thickening was present in 38.7% (214/552) of nerves examined. Clinico-electrophysiological dissociation between nerve thickening and nerve conduction findings was present in median, ulnar, great auricular, and common peroneal nerves.
Conclusion: Electrophysiological findings outnumber occurrence of nerve thickening and clinical deficits in leprous neuropathy. From a clinical perspective, enlargement of great auricular, ulnar, and common peroneal nerves may be more sensitive in predicting electrophysiological abnormalities.

Abbreviations: ANA, anti-nuclear antigen; ANOVA, analysis of variance; BB, mid borderline; BL, borderline lepromatous; BT, borderline tuberculoid; CMAP, compound muscle action potentials; CPN, common peroneal nerve; ESR, erythrocyte sedimentation rate; GAN, great auricular nerve; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HIV, human immunodeficiency virus; Hz, hertz; LL, lepromatous leprosy; mA, milli ampere; ms, milliseconds; mV, millivolts; N, pure neuritic; NCS, nerve conduction studies; SNAP, sensory nerve action potential; SPSS, Statistical Package for the Social Sciences; SSR, sympathetic skin response.

* Corresponding author. Tel.: +91 9559677084.
E-mail addresses: drneeraj2903@gmail.com (N. Kumar), drhsmalhotra@gmail.com (H.S. Malhotra), garg50@yahoo.com (R.K. Garg), rakesh_lalla@yahoo.com (R. Lalla), drkiranpreetmalhotra@yahoo.co.in (K.P. Malhotra), amita602002@yahoo.com (A. Jain), imranrizvi09@gmail.com (I. Rizvi).
[1] Tel.: +91 9450357392.
[2] Tel.: +91 9335901790.
[3] Tel.: +91 9044611842.
[4] Tel.: +91 8176007024.
[5] Tel.: +91 9415023928.
[6] Tel.: +91 9897246665.

http://dx.doi.org/10.1016/j.clinph.2016.05.002

Significance: A comprehensive nerve conduction study including great auricular and phrenic nerves, coupled with a sympathetic skin response, may aid in detecting cases with paucity of findings since such a combination is seldom seen in other disorders.

1. Introduction

Leprosy is a chronic granulomatous infection of skin and nerves caused by *Mycobacterium leprae*. It is the most common cause of acquired infectious neuropathy in the world, with India accounting for the maximum number of new cases of leprosy (Global leprosy situation, 2012). Though the skin manifestations cause unsightly dyspigmented patches, nodules, and deformed facial features (leonine facies), it is the nerve involvement that causes the maximum amount of disability in the form of loss of motor functions, skin ulcers, corneal ulcers, or major deformities of the limbs. Even skin changes, per se, are mostly secondary to dermal nerve involvement; pure neuritic form of leprosy may actually antedate the dermal lesions if the patients are closely followed (Suneetha et al., 2005). Loss of pigmentation is postulated to be due to either a decrease in synthesis or an impaired transfer of melanin in patients with leprosy. Importantly, most of the nerve dysfunction, if not detected early, remains largely irreversible.

Nerve conduction studies (NCS) may detect nerve dysfunction much earlier than the appearance of the symptoms and signs of nerve function impairment, as demonstrated in earlier studies (Vital et al., 2012; Chaurasia et al., 2011). In order to compare the predictive ability of clinical examination vis-à-vis NCS, we conducted a systematic and comprehensive electrophysiological evaluation of the nerves in patients with leprosy to look for clinico-electrophysiological correlation. Besides the conventional nerve conduction study protocol (median, ulnar, radial, common peroneal, posterior tibial, sural), an extended protocol was followed that involved the assessment of great auricular nerve, trigeminal nerve (blink reflex), facial nerve, and phrenic nerve, and the sympathetic skin response.

2. Materials and methods

2.1. Materials

This prospective study was conducted in the Department of Neurology, King George's Medical University, Lucknow, India, a tertiary care facility, from March 2012 to October 2013. The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from all patients before enrollment in the study.

Patients attending the out-patient department with features suggestive of neuropathy were screened for symptoms and signs of leprosy in a predesigned structured format to include sensory loss, hypopigmented patches, thickened nerves and neurological deficits. The suspected patients of leprosy were subjected to slit skin smear, nerve conduction studies, and sural nerve biopsy.

2.2. Methods

2.2.1. Clinical

Detailed evaluation of history and clinical examination was performed in all patients enrolled in the study. The *Daniels and Worthingham* functional grading system was used to score the deformities. The plan of the study is summarized in Fig. 1. Patients with history of chronic alcoholism or any other substance abuse were not evaluated. Patients were examined for the presence of thickened nerves: great auricular on the lateral aspect of the neck (better visible than palpable); the supraorbital nerve was palpated as it comes out of the notch on the forehead; the ulnar nerve was palpated behind the medial epicondyle in the ulnar groove; median nerve between the tendons of flexor compartment; superficial radial nerve running over the extensor pollicis tendon; common peroneal nerve around the neck of fibula; and, posterior tibial nerve below the medial malleolus (Donaghy, 2003). The palpation of nerves was independently done by two authors and only those nerves that were reported to be thickened by both authors were considered 'thickened'. Autonomic function was measured clinically as postural hypotension measuring fall in blood pressure (systolic $\geqslant$20 mmHg, diastolic $\geqslant$10 mmHg) at 1 or 3 min of standing.

Patients were examined for the presence of hypopigmented/hypoesthetic patches over the body. Wood's lamp examination was done to delineate the abnormal area. Hypopigmentation was defined as area of decreased skin color as compared to normal skin color in corresponding body area. Assessment of sensations was done for temperature (hot and cold) as well as for perception of touch and pain. The patients were also examined for any suggestion of type1 or type 2 lepra reactions.

The patients with skin lesions were classified into tuberculoid (TT), borderline tuberculoid (BT), mid borderline (BB), borderline lepromatous (BL) and lepromatous leprosy (LL) as per Ridley Jopling Classification; patients with only nerve involvement without any skin lesions, present or past, were labeled as having pure neuritic (N) form of leprosy. The nerve conduction studies were carried out in all patients. All patients enrolled in this study were subjected to complete blood count, erythrocyte sedimentation rate (ESR), fasting and post prandial blood sugars, renal function test, liver function test, anti-nuclear antigen (ANA) test, enzyme linked immunoassay for human deficiency virus, hepatitis-B antigen testing and anti-hepatitis C antibody testing.

Out of 79 consecutive patients screened, 46 patients fulfilling the criteria of leprosy based on clinical, histopathological and electrophysiological findings were included in this study. Except pure neuritic leprosy, all other cases were diagnosed and sub classified based on Ridley Jopling classification utilizing clinical and pathological findings. In pure neuritic leprosy, diagnosis was established based on nerve thickening, electrophysiology and supplemented by nerve and skin biopsy findings (Suneetha et al., 2001; Hui et al., 2015).

Of 33 patients not included in the study, 10 patients had diabetes mellitus, 2 were hepatitis-B antigen positive, 2 were HIV positive, 1 was ANA positive and 1 was positive for anti-HCV antibody. After slit smear examination, nerve and skin biopsy, and nerve conduction studies, 17 more patients were excluded owing to equivocal histopathology results.

All patients were treated with World Health Organization recommended multi-drug therapy regimen for appropriate duration along with supplemental steroids for 3–5 months.

2.2.2. Nerve conduction study protocol

All the nerve conduction studies were done on Medelec Synergy 5 channel EMG and EP system (VIASYS Health Care Systems, USA).