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Phrenic Nerve Conduction in Leprosy[1]

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Leprosy is characterized by involvement of the cutaneous sensory nerves and superficial nerve trunks. This predilection is explained by the fact that *Mycobacterium leprae* prefer cooler tissues for their growth ([18, 20]). Chronic granulomatous reaction leads to damage of all types of nerve fibers in the nerve trunk ([4, 8]). The signs and symptoms that characterize involvement of deep nerves are not usually seen in leprosy ([20]), although postural hypotension has occasionally been reported ([17]). The impairment of cardiovascular reflexes and the impairment of the cough reflex have been demonstrated in leprosy, suggesting vagus nerve involvement ([10–12]). The phrenic nerve, a deeply situated, predominantly motor nerve, is accessible for electrodiagnostic testing ([5, 13, 16]). Since the involvement of the phrenic nerve in leprosy has not been previously reported, the present study was carried out to determine the incidence and nature of phrenic nerve involvement in leprosy.

PATIENTS AND METHODS

There were 40 patients (33 males, 7 females), aged 16 to 80 years (mean 33.8 ± 14.02 S.D. years), who were attending the leprosy clinic of our institute and 25 control subjects (21 males, 4 females), aged 20 to 60 years (mean 34.7 ± 13.8 S.D. years). The patients were classified according to the Ridley-Jopling classification ([19]). There were 22 patients with borderline lepromatous to polar lepromatous leprosy (BL-LL) and 18 patients with borderline tuberculoid to polar tuberculoid leprosy (BT-TT). All patients and control subjects were nondiabetic and had no overt nutritional deficiency or history of chronic alcohol intake or occupational exposure to toxins. All gave their informed consent for the study.

Phrenic nerve conduction was carried out on a Medelec (MS 6) electromyograph according to the method described by Newsom-Davis ([16]). The nerve was stimulated on both sides of the neck at the posterior border of the sternamastoid muscle at the level of the upper border of the thyroid cartilage. The diaphragm compound muscle action potential (CMAP) was recorded by disc electrodes placed 4 to 5 cm apart in the ipsilateral eighth intercostal space in the anterior axillary line. A ground electrode was placed on the anterior chest wall between the stimulating and recording electrodes. A square wave pulse of 0.2 msec was applied at the rate of 1 Hz. With careful placement of the stimulating electrode, the diaphragm CMAP was obtained without a significant spread of the stimulus to the brachial plexus. The phrenic nerve conduction time (NCT), amplitude, and duration of CMAP were recorded. For comparison with peripheral nerves, the motor and sensory conduction of the median nerve was studied ([1, 3]), irrespective of its clinical involvement. Movements of the diaphragm were examined by fluoroscopy. Plus and minus 2.5 standard deviations (S.D.) of the mean control values were considered to be the normal limits for the various electrophysiological parameters of the phrenic nerve.

Statistical analyses were performed by the Student's *t* test and by analysis of variance.

RESULTS

A biphasic diaphragm CMAP with initial positive polarity was obtained (Fig. 1) in all control subjects (50 nerves) with a phrenic NCT of 7.47 ± 0.84 (mean ± S.D.) msec, an amplitude of 0.80 ± 0.22 mV, and a duration of 35.11 ± 4.37 msec. The phrenic NCT on the right and left sides was 7.54 ±

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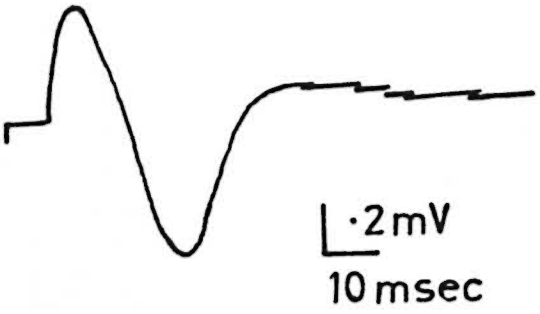

FIG. 1. Normal biphasic compound muscle action potential of the diaphragm on stimulation of the phrenic nerve.

0.88 msec and 7.40 ± 0.81 msec, respectively; the difference was not statistically significant. The difference in right and left phrenic NCT in individual control subjects ranged from 0 to 1.1 msec. A phrenic NCT of more than 9.60 msec, CMAP amplitude of less than 0.33 mV, and CMAP duration of more than 46.0 msec were taken as abnormal. One patient with a difference of 1.3 msec in the phrenic NCT between the right and left nerves was also considered abnormal, although his absolute NCT was normal on both sides.

Phrenic nerve conduction was found to be abnormal in 15 patients (19 nerves) out of 40 (37.5%), including 9 BL-LL patients (13 nerves, 4 bilateral) and 6 BT-TT patients (all unilateral). The abnormality was in the form of an increased NCT or a reduced CMAP amplitude or both. In the BL-LL group, the NCT was prolonged in 7 nerves and the CMAP amplitude was low in 9 nerves, while in the BT-TT group the amplitude was reduced in 5 nerves and the NCT was prolonged in only 1 nerve (Table 1, Fig. 2). The CMAP duration was not abnormal in any of the patients. A comparison of the mean values of the BL-LL and BT-TT groups with the control subjects revealed a prolonged NCT and a reduced CMAP amplitude in the BL-LL group; this was statistically significant. In the BT-TT group, only the CMAP amplitude was reduced, but the difference was not significant (Table 2).

Motor and/or sensory conduction of the median nerve was abnormal (motor conduction velocity < 45 m/sec, sensory action potential < 10 μV in amplitude or absent) in 16 BL-LL patients and six patients of the

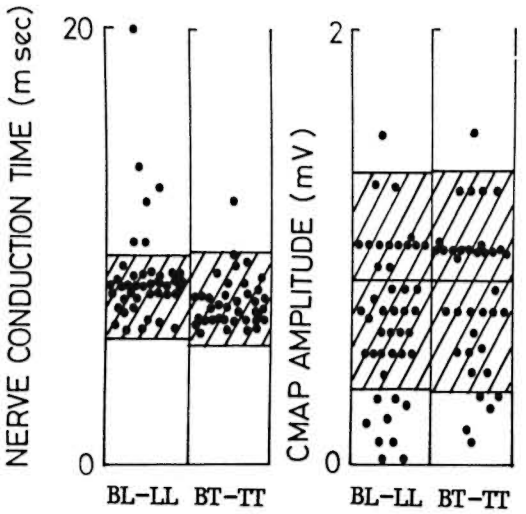

FIG. 2. Phrenic nerve conduction time and amplitude of compound muscle action potential (CMAP) in lepromatous (BL-LL) and tuberculoid (BT-TT) leprosy patients as compared to controls (▨ = mean ± 2.5 S.D.).

BT-TT group. Seven of the nine BL-LL patients with abnormal phrenic nerve conduction also had median nerve involvement, while only 2 out of 6 BT-TT patients with phrenic nerve involvement showed abnormal median nerve conduction. By fluoroscopic examination, movements of the diaphragm were normal in all patients.

DISCUSSION

Phrenic nerve conduction is a reliable electrodiagnostic test for the assessment of phrenic nerve function. Phrenic NCT, form, and the amplitude of the diaphragm CMAP obtained in the control subjects in the present study were similar to those reported by previous workers ([13, 16, 25]). Prolonged phrenic NCT as well as reduced amplitude of evoked diaphragm muscle response are recognized as indications of phrenic nerve involvement ([7, 13, 16, 24]). Abnormal phrenic nerve conduction has been reported in local lesions of the nerve as well as in generalized neuropathies such as Guillain-Barré syndrome, hereditary motor sensory neuropathy, and diabetic neuropathy ([7, 13, 15, 16, 25]).

Leprosy differs from other polyneuropathies by its predilection for superficial nerves. Intracutaneous nerves and parts of nerve trunks that lie closest to the surface of the body are preferentially involved, since

TABLE 1. *Results of phrenic nerve conduction in patients with lepromatous (22 BL-LL) and tuberculoid (18 BT-TT) leprosy.*

	Abnormal phrenic nerve function		
	BL-LL	BT-TT	Total
Patients	9	6	15
Nerves	13	6	19
NCT[a] prolonged	4	1	5
CMAP[b] amplitude reduced	6	5	11
NCT and amplitude abnormal	3	0	3

[a] NCT = nerve conduction time.
[b] CMAP = compound muscle action potential.

M. leprae requires a temperature of 27–30°C for its optimal growth ([18, 20, 22]). We found abnormal phrenic nerve conduction in 37.5% of leprosy patients. The involvement was more frequent in the BL-LL group, occurred bilaterally in four patients, and was associated with abnormality of the median nerve conduction in seven patients in this group. This observation probably reflects a more diffuse process in the lepromatous form of the disease as compared to tuberculoid leprosy. The BL-LL patients showed a significant abnormality in their phrenic NCT as well as in CMAP amplitude; the predominant abnormality in the BT-TT patients was in the form of reduced CMAP amplitude.

Slowing of nerve conduction in the BL-LL patients may be attributed to segmental demyelination and/or loss of nerve fibers, especially large myelinated fibers ([2, 6, 8, 20, 21]). Axonal loss may also explain the reduced CMAP amplitude. On the other hand, a tuberculoid granuloma may destroy only a part of a few funiculi of a nerve trunk ([8]), and the remaining fibers may conduct normally. The reduced CMAP amplitude can be associated with normal NCT, as was observed in the BT-TT group of the present study.

Phrenic nerve involvement in leprosy appears to be subclinical since diaphragm movements on fluoroscopic examination were normal in all patients. Various conduction studies on different nerves in leprosy have revealed slow conduction in some of the clinically normal nerves and sometimes even in the asymptomatic contacts of leprosy patients ([6, 14, 20, 21]). The route of involvement of the phrenic nerve in leprosy is a matter of conjecture. It could be hematogenous or by direct spread from some superficial nerve. The phrenic nerve has no recognized connection with any superficial nerve trunk(s). Sensory fibers carried in the phrenic nerve supply mainly the mediastinal pleura, pericardium, parietal pleura, and parietal peritoneum above and below the central part of the diaphragm. The nerve receives inconstant communicating filaments from cervical sympathetic ganglia, and may also communicate with internal mammary sympathetic fibers ([23]). None of these connections appears significant for the spread of the leprosy bacilli. On the other hand, bacillemia and visceral involvement in leprosy, particularly in the lepromatous form, has been reported ([4, 8, 9]), and phrenic nerve involvement may also be due to hematogenous spread.

SUMMARY

Phrenic nerve conduction was performed bilaterally in 22 multibacillary (BL-LL) and 18 paucibacillary (BT-TT) leprosy patients and 25 control subjects. Prolonged phrenic nerve conduction time and/or reduced amplitude of diaphragm muscle action potential beyond 2.5 standard deviations of control mean values was observed in 9 BL-LL patients (4 bilateral) and 6 BT-TT patients

TABLE 2. *Phrenic nerve conduction in control subjects and patients with leprosy.*

Parameter	Controls (N[a] = 50)	BL-LL (N = 44)	BT-TT (N = 36)
Nerve conduction time (msec)	7.47 ± 0.84	8.33[b] ± 2.37	7.38 ± 1.20
CMAP[c] amplitude (mV)	0.88 ± 0.22	0.68[b] ± 0.38	0.79 ± 0.34
CMAP duration (msec)	35.11 ± 4.37	35.49 ± 6.47	33.34 ± 4.07

[a] N = number of nerves.
[b] $p < 0.01$.
[c] CMAP = compound muscle action potential.

(all unilateral). Out of the nine BL-LL patients with phrenic nerve involvement, median motor and/or sensory nerve conduction was also abnormal in seven patients. On fluoroscopy, diaphragm movements were normal in all patients. The study documents subclinical phrenic nerve involvement in leprosy—a fact not previously recognized.

RESUMEN

Veintidos pacientes con lepra multibacilar (LL-BL), 18 con lepra paucibacilar y 25 personas sanas, mostraron conducción bilateral del nervio frénico. Se observaron valores prolongados de conducción del nervio frénico y/o una amplitud reducida del potencial de acción del músculo diafragmático mayor de 2.5 desviaciones estándar sobre los valores normales en 9 pacientes LL-BL (4 bilateral) y en 6 pacientes BT-TT (todos unilaterales). De los 9 pacientes LL-BL con afección del nervio frénico, 7 pacientes tuvieron también una anormal conducción motora y/o sensorial del nervio mediano. Por fluoroscopía, se encontró que los movimientos del diafragma fueron normales en todos los pacientes. El estudio documenta la afección subclínica del nervio frénico en lepra—un hecho no reconocido previamente.

RÉSUMÉ

On a étudié la conduction du nerf phrénique, des deux côtés, chez 22 malades multibacillaires (LL-BL) et chez 18 malades paucibacillaires (TT-BT), de même que chez 25 sujets témoins. Chez 9 malades LL-BL (et ceci chez 4 de façon bilatérale), et 6 malades BT-TT (tous de manière bilatérale), on a observé soit une prolongation du temps de conduction du nerf phrénique, soit une réduction de l'amplitude du potentiel d'action du diaphragme dépassant 2,5 écart-type de la moyenne, ou bien les deux phénomènes à la fois. Parmi les neuf malades LL-BL présentant une atteinte du nerf phrénique, on a relevé une conduction anormale au niveau du nerf moteur médian, ou des nerfs de la sensibilité, ou des deux à la fois. A la fluoroscopie, les mouvements du diaphragme étaient normaux chez tous les malades. Cette étude met en évidence une atteinte sous-clinique du nerf phrénique dans la lèpre, un phénomène qui n'avait pas été reconnu auparavant.

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