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Peripheral neuropathy in systemic lupus erythematosus - electrophysiological features in 50 consecutive patients

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Abstract

50 consecutive inpatients with systemic lupus erythematosus (SLE) were studied using nerve conduction studies and electromyography to determine the prevalence and pattern of peripheral neuropathy. The patients had no other known cause of peripheral neuropathy except SLE. 28% had clinical signs of peripheral neuropathy. The frequency of abnormal electrophysiological findings was 56%. The frequency of polyneuropathy (defined as abnormality in 2 or more nerves) was 42% of which two thirds had diffuse polyneuropathy and one third had multiple mononeuropathy. The most common abnormal electrophysiological parameter was a prolonged H reflex followed by reduced amplitude of compound muscle action potentials. Overall electrophysiological features suggest axonal degeneration rather than demyelination. Subclinical peripheral neuropathy is common in systemic lupus erythematosus.

Keywords: Lupus erythematosus, systemic; polyneuritis, neural conduction, electromyography

INTRODUCTION

Systemic lupus erythematosus (SLE) is a common autoimmune disease in Southeast Asia with multiple organ involvement. Neurological disease have frequently been observed but this has largely been central nervous system or psychiatric manifestations. The percentage of neurological involvement in reported series of patients in this part of the world have ranged from 10.4% to about 39.5%[1,2,3,4] but these have centered mainly upon the presence of seizures or psychosis. Disease of the peripheral nerve in SLE have rarely been studied exclusively, variously reported to range from 7 to 24% of patients[5,6,7,8,9,10] depending on the criteria used to define peripheral neuropathy. The relatively low incidence of peripheral nerve disease in earlier series[5,6,7] is likely to be because peripheral neuropathy was defined clinically rather than electrophysiologically. Studies based on electrophysiolgical criteria have yielded higher results[8,9,10]. Furthermore, the pattern of peripheral nerve involvement in SLE has not been well characterised and its underlying pathophysiology not well understood although an autoimmune or a vasculitic process seem likely.

We sought to evaluate patients with systemic lupus erythematosus for presence of peripheral neuropathy using nerve conduction studies and electromyography and to determine the pattern of peripheral nerve involvement.

MATERIALS AND METHODS

50 consecutive patients which fulfilled the American College of Rheumatology (ACR) criteria for SLE[11] who were admitted to the University Hospital, Kuala Lumpur were recruited in this study. Apart from the usual history and physical examination, a full neurological examination by a neurologist was carried out. Clinical signs of peripheral neuropathy were noted. Exclusion criteria were the presence of diabetes mellitus, chronic renal failure and any other known cause of peripheral neuropathy.

All patients studied were female. Their ages ranged from 12 to 52 years with a mean age of 29.9 years. The mean duration of SLE was 4.2 years with the range from 2 months to 23 years. Disease activity was measured using the Lupus Activity Criteria Count (LACC)[12]. The clinical and laboratory features of our patients are summarised in Table 1. The patients had involvement of various systems but none were admitted primarily for a neurological (central or peripheral) disorder. Student's t test was used to determine statistical difference between the peripheral neuropathy and non-peripheral neuropathy groups with regards to disease activity.

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TABLE 1: Clinical and laboratory characteristics of the study patients. *LACC (Lupus Activity Criteria Count) score ≥ 2 [12]

Clinical and laboratory features	% of patients
Skin involvement	45.6
Oral ulcers	2.2
Arthritis	56.5
Nephritis	60.9
Serositis	17.4
Haematological involvement	50.0
Raynaud's phenomenon	6.5
Vasculitis	39.1
Active disease *	74.0
Positive ANA	100.0
Positive anti-ds DNA	90.0
Positive anticardiolipin antibody	60.0

Nerve conduction studies

Nerve conduction studies were carried on a Neuromatic 2000 electromyography machine (DISA). Surface stimulating and recording electrodes were used. The study was carried out in an open room, and in our country, it is unnecessary to warm the limbs of our subjects to maintain the skin temperature above 32 °C. The following nerves were studied bilaterally - median (motor and sensory), ulnar (motor and sensory), radial (sensory), posterior tibial and common peroneal. F waves (minimum latency) of median and ulnar nerves were also measured bilaterally. The soleal H reflex was measured in 19 patients. Normal values for our laboratory were obtained previously and an abnormal value was defined as ± 2.5 standard deviation above/ below the laboratory's normal mean.

Electromyography

Standard concentric needle electromyography of the abductor pollicis brevis and abductor digiti minimi were carried bilaterally.

Definitions

Involvement of one peripheral nerve only defined a mononeuropathy. Abnormality in two or more nerves defined a peripheral neuropathy electrophysiologically[13]. If the pattern was symmetrical, this suggested a diffuse polyneuropathy while an asymmetrical involvement suggested a mononeuropathy multiplex.

RESULTS

Clinically, 14 patients (28%) had objective signs of peripheral neuropathy. Seven had absent or reduced deep tendon reflexes in the lower limbs, three had intrinsic muscle wasting, three had both reduced reflexes and intrinsic muscle wasting and one patient had clinically a left sciatic nerve palsy (although electrophysiologically she had a more widespread involvement).

Twenty eight patients (56%) had abnormality on nerve conduction studies and/or electromyography. Seven patients (14%) had abnormal parameters of one nerve only viz. three ulnar, three median (of which one fulfilled the criteria for a carpal tunnel syndrome) and one with an absent H reflex only.

Taking the abnormality of two or more nerves as the electrophysiological criteria for polyneuropathy, then 21 patients (42%) had polyneuropathy. Asymmetrical involvement suggesting mononeuropathy multiplex was seen in seven of these patients while 14 had symmetrical involvement suggestive of diffuse polyneuropathy. One patient had absent knee and ankle reflexes but had normal electrophysiological studies. There was no statistical significant difference in disease activity (as defined by a LACC score ≥ 2) between the peripheral neuropathy and the non peripheral neuropathy group.

The frequency of abnormality in the various nerve conduction parameters studied are summarised in table 1. Although the soleal H reflex was studied in only 19 of our patients, it appears to be the most frequently abnormal parameter (28.9%). F wave latency was prolonged or absent 4.5% of the time. In three patients, the late responses were the only abnormality found (two H reflex, one F wave). Compound muscle action potential (CMAP) amplitude were reduced in 14% while the sensory nerve action potential (SNAP) amplitude were diminished in 9.7% of tests. Distal latency measurement (motor and sensory) and nerve conduction velocity were less often abnormal. These findings suggest a predominantly axonal form of neuropathy. No patient had electrophysiological features suggesting a demyelinating neuropathy.

Needle electromyography was abnormal in 8% of the muscle studied. These consisted of spontaneous activity (fibrillations, positive sharp waves and complex repetitive discharges) in 12 muscles studied and reduced recruitment and

TABLE 2: Percent (abnormal to total no. of tests) of nerve conduction parameters in 50 SLE patients that were abnormal (i.e. 2.5 SD above/below the normal mean).

	Median Nerve	Ulnar Nerve	Radial Nerve	Peroneal Nerve	Tibial Nerve	Total
CMAP* amplitude	10% (10/100)	13% (13/100)	n.a.	25% (25/100)	8% (8/100)	14% (56/400)
SNAP* amplitude	14% (14/100)	14% (14/100)	1% (1/100)	n.a.	n.a.	9.7% (29/00)
Distal Motor Latency	3% (3/100)	0%	n.a.	0%	0%	0.8% (3/400)
Distal Sensory Latency (onset)	1% (1/100)	0%	0%	n.a.	n.a.	0.3% (1/300)
Motor velocity	3% (3/100)	5% (5/100)	n.a.	2% (2/100)	n.a. (3/100)	3.3% (13/400)
Sensory velocity	3% (3/100)	2% (2/100)	0%	n.a.	n.a.	1.7% (5/300)
F Response	7% (7/100)	2% (2/100)	n.a.	n.a.	n.a.	4.5% (9/200)
H Reflex	n.a.	n.a.	n.a.	n.a.	28.9% (11/38)	28.9% (11/38)
EMG*	9% (9/100)	7% (7/100)	n.a.	n.a.	n.a.	8% (16/200)

* CMAP = compound muscle action potential,
SNAP = sensory nerve action potential,
EMG = needle electromyography of abductor pollicis brevis (median nerve), abductor digiti minimi (ulnar nerve)
n.a. = not applicable

broad polyphasic motor units only in another four muscles. None had myopathic features.

DISCUSSION

The frequency and pattern of peripheral neuropathy in our series of inpatients with SLE were evaluated. Although clinically 28% of our patients had signs to suggest peripheral neuropathy, electrophysiologically 56% had abnormal nerve conduction studies and 42% had (by definition of 2 abnormal nerves or more) polyneuropathy. This clearly suggests that a sizable proportion of patients have subclinical peripheral nerve disease. As other known causes of peripheral neuropathy have been excluded, it is likely that SLE may be the cause of the peripheral neuropathy. The prevalence of peripheral nerve disease in our series of patients are much higher compared to previous reports of SLE neuropathy (ranging from 20 - 27%)[8,9,10]. Two of these studies had much smaller sample size (33 and 34 patients respectively) and were carried out in Europeans and therefore racial differences in disease expression may account for the discrepancy. In addition our patients were younger (mean age 29.9 years vs. 42.5/43 years) and had a shorter duration of disease (mean duration 4.2 years vs. 12.5/12 years). Tan *et al* from Singapore reported a prevalence of peripheral neuropathy of 20% in 60 unselected SLE inpatients[9] which is lower than our present series of patients. Nerve conduction studies were carried out unilaterally in their patients and this could account for the lower prevalence in a peripheral nerve disorder which may sometimes be patchy and multifocal.

One possible criticism of the present study is that external nerve compression may be a cause of neuropathy in inpatients who may be bedridden. Our patients were however on the whole not severely disabled neurologically (none had any clinical central nervous system disease) and all were ambulant. This makes neuropathy due to compression less likely, although this question only be effectively resolved with a case-control study using age and sex matched inpatient controls.

Peripheral neuropathy in systemic lupus erythematosus has often been described as a

chronic polyneuropathy with predominantly sensory features or focal mononeuropathy or multiple mononeuropathy [5,6,7,14] . In addition there may be associated immune mediated neuropathies such as the Guillain-Barre syndrome and chronic inflammatory demyelinating polyneuropathy (CIDP)[15,16,17]. Pathophysiological mechanisms may therefore be heterogeneous. Histopathological findings have varied from axonal degeneration with or without vasculitis[6,14] to demyelination in patients with associated immune mediated neuropathies[15]. In our patients the most common pattern of neuropathy was that of a diffuse polyneuropathy (28%). Seven patients (14%) each had features of focal mononeuropathy and multiple mononeuropathy respectively. None presented with neuropathic symptoms suggesting an immune mediated neuropathy such as Guillain-Barre syndrome or CIDP.

The most common abnormal parameters are a prolonged or absent H reflex followed by reduced action potential amplitudes. Distal latency and conduction velocity were less often affected. The frequently abnormal late responses suggest that in our patients the proximal nerve segment may be prominently involved. This may suggest that the underlying pathophysiological mechanism affecting the nerves do so in a patchy manner rather than through a 'dying back' phenomenon as seen in most metabolic neuropathies in which distal abnormalities are more severe. This may be consistent multifocal process such as a vasculitis causing destructive changes in the small blood vessels, immune complex deposition or antibody mediated damage - the proposed mechanisms for neuropathy in connective tissue disorders[18]. In addition, reduced action potential amplitudes suggest an axonal rather than demyelinating neuropathy, again consistent with previous histopathological studies[14]. An interesting finding was that motor nerve parameters were more frequently abnormal compared to sensory parameters and needle electromyography was abnormal in 8% of the time. Therefore SLE neuropathy is not necessarily mainly a sensory neuropathy and may have prominent motor involvement.

Subclinical peripheral neuropathy in systemic lupus erythematosus is common. Unlike other well-characterised immune-mediated neuropathies, it is mainly an axonal neuropathy with evidence of diffuse or multifocal involvement. The significance of the presence of neuropathy detected electrophysiologically is uncertain. There is no significant association with disease activity. The relationship to other organ involvement and prognosis would need to be investigated further. Whether it will progress to clinical neurological disease and whether early aggressive therapy may retard progression are questions that need to be answered.

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