Received 09 January 2024 | Accepted 12 February 2024
DOI: https://doi.org/10.4038/sljon.v10i2.163

SLJoN

ORIGINAL ARTICLE

Sural nerve involvement in patients with acute inflammatory demyelinating polyneuropathy variant of Guillain-Barre syndrome with sural sparing at initial presentation

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Abstract

Introduction: Neurophysiological testing is a valuable tool in the diagnosis of Guillain-Barre syndrome (GBS). Sural sparing is a usual feature of acute inflammatory demyelinating polyneuropathy (AIDP) type GBS. However, sural involvement has been reported in later stages of GBS. It is important to identify patterns of sural nerve involvement to differentiate GBS from its mimickers and to stage the disease. This research aimed to detect the pattern of sural nerve involvement in AIDP-GBS cases with normal electrophysiological responses in the sural nerve at the beginning.

Objectives: To determine the location and timing of sural nerve involvement in AIDP-GBS.

Methods: This prospective follow up study included diagnosed cases of AIDP-GBS with preserved bilateral sural responses. Nerve conduction and somatosensory evoked potentials (SSEP) were done on admission and weekly thereafter for four consecutive weeks. The last evaluation was done four weeks after the fourth study.

Results: All patients (100%) showed normal distal sural responses over the initial four weeks of follow up. They continued to remain normal up to eight weeks in eight patients (53.3%). Two patients had gradual prolongation of their sural SSEP on consecutive studies. One of them had gradual reduction of sural sensory nerve action potential and nerve conduction velocity along with the prolongation of sural SSEP latencies. The difference of SSEP latency increments in the left sural nerve of these two patients was statistically significant ($p<0.05$). The right sural SSEP latency difference was not significant.

Conclusion: Sparing of the distal sural sensory response was demonstrated in 100% of AIDP-GBS cases during the first four weeks of follow up. More than 50% of the cohort demonstrated preserved sural sensory responses for eight weeks from the initial presentation. Two out of fifteen patients showed statistically significant proximal sural sensory pathway involvement with increasing SSEP latencies. This finding suggests that in some patients, the sural sensory pathway may get affected at its proximal segments or at the central nervous system before the distal nerve is affected.

KEYWORDS
Somatosensory evoked potential, nerve conduction study, sural sparing

INTRODUCTION

Guillain-Barre syndrome (GBS) is the leading cause of acute inflammatory demyelinating polyneuropathy (AIDP) in the world. Though the diagnosis is based on the clinical features; electrodiagnostic testing or nerve conduction studies (NCS) help to increase the diagnostic accuracy. Serial NCS in patients with GBS can help to identify the pattern of nerve involvement. It also helps to evaluate the treatment outcome.[1] Routine peripheral NCS in AIDP-GBS shows features of demyelination such as increased latencies, decreased conduction velocities, temporal dispersion, and conduction blocks.[2] While sparing of the distal sural sensory response is an expected neurophysiological finding in early AIDP, reduced or absent sural sensory response can be an early feature of GBS mimickers such as acute onset chronic inflammatory demyelinating polyneuropathy (CIDP). Therefore, evaluating the pattern of sural involvement in GBS helps to identify the neurophysiological pattern of disease progression over time. This study attempted to identify the timing and location of sural nerve involvement in patients with AIDP and to describe precipitating events, presenting neurological features, and response to treatment.

METHODOLOGY

This is a prospective follow up study conducted at the neurology and general medicine wards of the National Hospital of Sri Lanka, Colombo from December 2019 to November 2020. Patients above the age of 18, with diagnosed GBS with normal sural sensory responses at initial presentation were included in the study. These patients were diagnosed according to the consensus guideline by Leonhard et al., for the diagnosis and management of GBS.[3] Patients not compliant with repeated electrodiagnostic studies and patients in respiratory distress were excluded.

An interviewer-administered questionnaire and inward medical records were used for data collection. NCS and somatosensory evoked potentials (SSEP) were conducted on admission and weekly thereafter up to four weeks if the distal sural sensory nerve conduction was normal in the study prior. The last NCS and SSEP were done eight weeks from the first study. Posterior tibial, peroneal, median, ulnar, sural, and radial nerve conduction studies were performed with relevant F-waves. In the presence of normal distal sural sensory responses, sural SSEPs were done at every visit. Tibial SSEP was performed for the convenience of interpretation of test results. All NCS were conducted by a specialty trainee in clinical neurophysiology. The sural sensory response was recorded posterior to the lateral malleolus of the lower limb and the stimulation site was 10 cm away from the recording electrode. The leg temperature was maintained at or above 30° Celsius. All the SSEP were conducted by a senior experienced neurophysiologist to prevent operator bias. Sural SSEP were done by stimulating the skin posterior to the lateral malleolus. Cortical latencies were recorded over Cz prime cortical area according to the 10-20 international system.[4,5]

In the absence of standard thresholds for sural sensory nerve actional potential (SNAP) and nerve conduction velocity (NCV) for Sri Lankan population; we used the cutoff as six micro vaults (μV) for SNAP and 40 m/s for NCV.[6,7] Distal sural response was considered as spared if both SNAP and NCV were same or above the cutoff levels. Sural SSEP latencies were assumed to be equal to tibial SSEP latencies as the distance between stimulation and cortical recording is almost equal. We analyzed the mean of the longitudinally measured sural amplitude and velocity using one sample T test (95% confidence interval). Data was analyzed using SPSS software, version 25.0. Standard descriptive methods including frequencies, percentages, means, and standard deviation (SD) were used to describe the data. Significance of associations was calculated using Chi square test/ Fishers exact test and T test. A p value < 0.05 was considered statistically significant.

Ethical approval was obtained from the Ethical Review Committee of the National Hospital of Sri Lanka, Colombo.

RESULTS

The sample included fifteen consecutive participants satisfying the above criteria.

Of the fifteen patients, the majority were males (86.7%). Their ages ranged from 23 to 66 years (mean age 41.47±11.9). Two patients (13.3%) had type 2 diabetes mellitus, one (6.7%) had a previous diagnosis of bilateral carpal tunnel syndrome. No patient had a previous history of neuromuscular disorders.

Seven patients (46.7%) gave a history of preceding events within four weeks of symptom onset. Six (40%) had either a preceding respiratory tract infection (20%) or a diarrhoeal illness (20%). One (6.7%) gave a history of a road traffic accident with minor trauma. None gave a history of preceding vaccination or surgery.

The presenting neurological deficit in the majority was weakness in the upper or lower limbs (86.7%). Cranial nerve involvement was observed in 20% at the first clinical encounter. All fifteen patients (100%) showed protein-cellular dissociation in cerebrospinal fluid (CSF) analysis on day 10 from symptom onset.

All fifteen patients were treated with intravenous immunoglobulin (IVIg), continued for five days according to the local guidelines. The mean duration from onset of symptoms to start of IVIg was 8.3±7.3 days. Treatment response was demonstrated as improvement in neurological weakness by at least one grade on the modified Rankin Scale (mRS) after completing five days of IVIg. This was assessed on the day after

completion of the last IVIg dose. Thirteen (86.7%) showed a satisfactory improvement following completion of IVIg while two patients (13.3%) did not show improvement in their neurological weakness.

All fifteen patients (100%) had their sural SNAP (mean 18.82±11.14μV) and NCV (mean 47.2±2.45m/s) preserved over the initial four weeks of follow up. Only eight presented themselves for the fifth assessment of NCS and SSEP in the eighth week. The distal sural response remained preserved in all of them. SSEP latencies remained unchanged in thirteen patients (86.7%) in the initial four weeks period, while two (P1 and P9) showed gradual prolongation of it on either side. P1 showed a gradual decrement in sural amplitude and NCV on both sides (Table 1). However, the sural SNAP and NCV of this patient were above the cut off levels throughout the study. The difference in left sural SSEP latencies of these two patients (P1and P9) was statistically significant ($p < 0.05$). The difference in right sural SSEP latencies was not statistically significant (Figure 1).

On retrospective analysis of patients' histories, P1 and P9 were 50 and 49 years old, respectively. P1 had a history of type 2 diabetic mellitus, whereas P9 had no medical problems in the past. Out of the two, P9 had a preceding respiratory tract infection. P1 presented with bilateral facial nerve palsy as the presenting neurological symptom while P9 presented with symmetrical lower limb weakness. P1 and P9 had received IVIg on day five and on day ten from their symptom onset respectively. The delay in starting IVIg in P9 was due to the delay in presentation to the hospital. Despite increasing sural SSEP latencies, both these patients showed a satisfactory improvement in their neurological weakness on the mRS scale.

TABLE 1 **Mean sural SNAP, NCV and SSEP latencies of consecutive measurements in all the visits**

Case number	Mean sural SNAP (μV)		Mean sural NCV(m/s)		Mean sural SSEP latency(ms)	
Side	**L**	**R**	**L**	**R**	**L**	**R**
P1	17.08	16.12	45	46.5	60.3	64.9
P2	21.4	17.8	48.5	47.5	41.3	41.4
P3	11.26	13	50	50	55.5	53.5
P4	30.9	32.54	46.5	47.5	48.5	48
P5	16.9	20.66	44	43	49.5	50.5
P6	16	20	48.5	50	49.8	50.7
P7	7.06	9.8	43.5	44.5	50	51.1
P8	8.46	8.85	43.5	43	49.2	49.8
P9	14.52	16	48.5	47.5	54	52.2
P10	28	28.8	50.5	49.5	48.3	50.4
P11	10.12	12.3	50.5	50	49.7	49.1
P12	16.2	17.38	46.5	44.5	47.9	49.9
P13	14.4	14.44	49.5	50	47.2	48.2
P14	20.8	16.8	43.5	41.5	42.1	42.8
P15	31.08	33.72	49.5	49.5	46.6	46.5

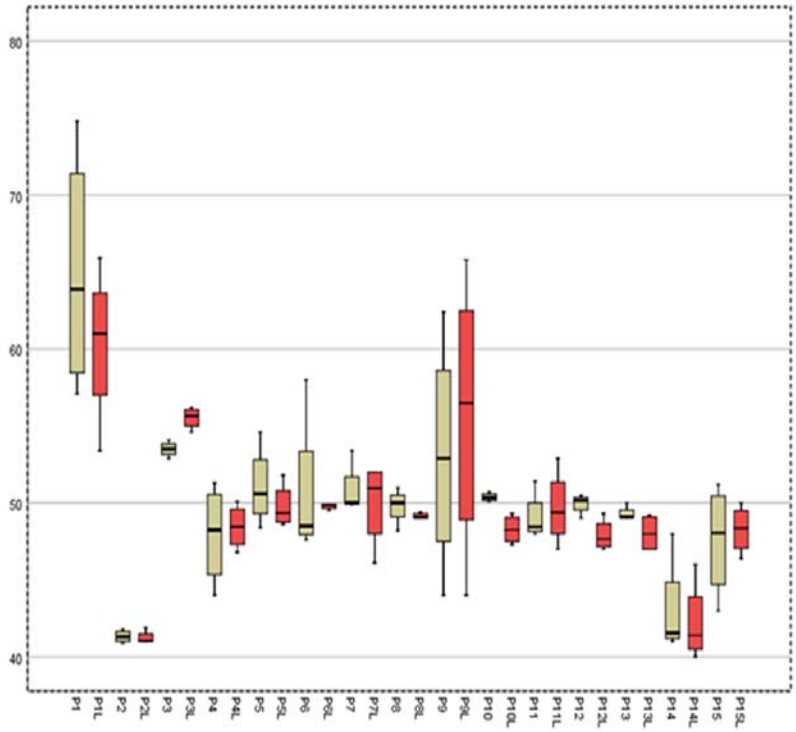

FIGURE 1 **Boxplots showing the degree of variation in sural SSEP latencies of each patient in subsequent visits: Brown- right side; Red- left side.**

DISCUSSION

Our study shows a sural sparing pattern in all cases (100%) in the first four weeks of follow up. This was further demonstrated in all patients who underwent their fifth neurophysiological evaluation at eight weeks from the first study. Thirteen patients (86.7%) showed no significant difference in SSEP latencies in the initial four weeks of follow up. Two patients (13.3%) demonstrated gradual prolongation of sural SSEP latencies despite normal distal sural nerve conduction. One of these patients showed gradual decrement in sural amplitude and nerve conduction velocity within the normal range.

A retrospective study by Gordon et al. described that a definitive diagnosis of GBS is difficult in the initial few days of disease onset[1]. This is partly related to the neurophysiological findings not meeting the diagnostic criteria in the initial stages of the disease.[2] Thus, longitudinal assessment of nerve conduction studies during the illness is suggested.[8] Relative sural sparing may be evident in the electrodiagnostic studies of AIDP variant GBS in the initial stages, but may become less evident on follow-up studies.[9] The pattern of sural nerve involvement in diagnosis of AIDP variant GBS, is useful to differentiate GBS from its mimickers. In AIDP variant GBS, the sural sensory nerve frequently shows normal neurophysiological findings. In certain types of polyneuropathies, median and ulnar sensory nerves become affected early, while in some other types, the sural sensory nerve is the first to become affected.[10] However, previous studies have described a deviation from this common pattern by involvement of the sural nerve in a minority of GBS patients[11]. A retrospective study had analyzed the relative sparing of sensory nerves and their ratios in AIDP patients two weeks from symptom onset. This had shown the sural sparing pattern was present only in AIDP variant GBS. They evaluated the sural/radial sensory ratio which is considered as a useful independent predictor of AIDP[12]. Our finding of sural sparing adds further evidence to the current understanding of preserved sural responses in early AIDP-GBS. The sural sparing demonstrated at eight weeks after hospital admission indicates that this feature may be present even beyond the initial stages of the disease.

The causes or risk factors for sural nerve involvement are not well described. Older age is shown to be associated with sural nerve involvement in GBS.[11] A prospective cohort study had shown age ≥50 years is an independent factor for sural nerve compromise on admission.[11] The age range for our cohort was 23 to 66 years with a mean age of 41.47±11.9 years. The two patients (P1 and P9) who showed subsequent proximal sural sensory pathway involvement were 50 and 49 years in age, respectively.

Some studies favour the fact that sural nerve involvement present in minority is a bad prognostic factor,[12] while other studies describe the inverse.[11] IVIg is the most frequently used treatment for GBS.[13] We assessed the patients

neurologically before and after completion of IVIg. Thirteen patients (86.7%) showed a satisfactory response to IVIg on the modified Rankin scale. The two patients in our cohort who had increasing sural SSEP latencies, also had good response to IVIg therapy despite possible evidence of proximal sensory pathway involvement. The difference in left sural SSEP latencies of these two patients were statistically significant ($p<0.05$) compared to the rest of the population, while the right sural SSEP latency difference was not significant (Figure 1). Even though this statistical significance excludes inter-trial variations, these findings again could have been affected by immunoglobulin therapy. As immunoglobulins halt the progression of the disease process, the effect of this standard therapy would have masked neurophysiological progression.

This study is a single centered study, raising the question of generalisability to the entire population. The sample size was limited to fifteen patients due to the COVID-19 pandemic and reduced number of hospital admissions. Seven patients did not attend the planned fifth neurophysiological assessment. The pattern of sural nerve involvement may have been affected by treatment.

CONCLUSION

Normal distal sural sensory response is an important positive neurophysiological finding in AIDP variant GBS. In this study, this was neurophysiologically demonstrable up to eight weeks from hospital admission. Gradually increasing sural SSEP latencies with normal distal sural sensory responses may suggest initial proximal sural sensory pathway involvement in AIDP variant GBS. This proximal sensory involvement could be at the level of peripheral nerve/root or at central pathway. Gradual decrement of sural SNAP and NCV along with increasing sural SSEP cortical latencies could be a manifestation of impending distal sural nerve involvement.

Conflicts of interest

None.

ACKNOWLEDGMENTS

We thank all the patients who participated and their families.

We also thank all the staff members of the Department of Clinical Neurophysiology at the National Hospital of Sri Lanka for their support.

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