ELECTROPHYSIOLOGICAL FINDINGS IN EARLY GUILAIN-BARRÉ SYNDROME

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SUMMARY – The aim of the study was to identify the most common electrophysiological abnormalities in early Guillain-Barré syndrome (GBS). Neurophysiological data on 51 GBS patients assessed within 12 days of symptom onset were reviewed. Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) was present in 46 of 51 GBS patients. The following abnormalities were observed in our AIDP patients: absent H reflex in 90.7%, conduction block in the Erb-to-axilla segment in 78.6%, motor conduction velocity suggestive of demyelination in the Erb-to-axilla segment in 45.2%, prolonged F wave latency in 65.2%-73.8% of patients but only 20.0%-37.0% with prolonged F wave latency suggestive of demyelination, and reduced or absent sensory nerve action potential in 62% of patients. Abnormal values of terminal latencies, and motor and sensory conduction velocities in distal nerve segments suggestive of demyelination were recorded in less than 30% of patients. In conclusion, the most sensitive parameter in early GBS patients is conduction block in the most proximal segments of the peripheral nervous system, directly determined in the Erb-to-axilla segment or indirectly as absent H reflex. Motor conduction studies in the Erb-to-axilla segment are very informative in early GBS patients.

Key words: Guillain-Barré syndrome; Neural conduction; Electromyography

Introduction

Early diagnosis of the Guillain-Barré syndrome (GBS) is important since several treatments have been shown to diminish the disease severity and improve the outcome. Electrophysiological studies in GBS have been reported by a number of authors and have been found useful in diagnosing the condition¹-⁴. The aim of this study was to identify the most common electrophysiological abnormalities early in the course of GBS.

Early electrophysiological confirmation of the diagnosis is even more important as the cerebrospinal fluid protein level may frequently be normal within the first week. However, the electrophysiological finding varies in the same patient during the course of disease and characteristic abnormalities may not evolve for several days or weeks⁵.

Methods

We reviewed medical records of all patients with a confirmed clinical and laboratory diagnosis of GBS, admitted to our department during the past 20 years. Only patients submitted to electrodiagnostic testing within 12 days (range 2-12 days) of the onset of symptoms were selected for the study. All recruited patients met the standard diagnostic criteria for GBS⁶,⁷. Patients with diabetes mellitus, systemic disease, chronic alcohol abuse, and other causes of chronic acquired neuropathy were excluded.

Electrophysiological studies were performed on a Medelec Mistro and Medelec Synergy electromyography machine. All patients were studied in the same
EMNG laboratory at our Department and all studies were performed by the same two electromyographers. The standardized techniques and protocols were used.

Motor and sensory conduction studies were performed using the standard technique of supramaximal percutaneous stimulation and surface electrode or concentric needle electrode recording. Distal latencies and motor conduction velocities (MCV) were measured in the median, ulnar and deep peroneal nerves. Stimulus sites for the common peroneal nerve were at the ankle and fibular head with recording from the short extensor muscle of the toe. Median nerve was stimulated at 4 sites (at the wrist, elbow, axilla and Erb’s point) with recording of the compound motor action potential (CMAP) from the short abductor muscle of thumb (Fig. 1). Ulnar nerve was stimulated at 5 sites (at the wrist, below and above the elbow, axilla and Erb’s point) with CMAP recording from the abductor muscle of little finger. CMAP amplitude was systematically analyzed only in the last 28 patients. To ensure supramaximal stimulation at Erb’s point, maximal CMAP amplitude had to be achieved with stimulus intensity being lower than maximal stimulator output. Supramaximal stimulation at Erb’s point could not be achieved in four of 51 patients. Determination of distance from Erb’s point to the point of stimulation in the axilla may contain some error. Therefore, the distance was callipered to ensure correct measurement.

Deep peroneal nerve was stimulated at the ankle and knee, and CMAP was recorded in the short extensor muscle of toe. CMAP amplitudes were measured from baseline to negative peak and CMAP latencies to the beginning of the potential.

F waves were obtained at the distal motor stimulation point and minimal latency of 10 consecutive stimulations was recorded. The H reflex was recorded from the soleus muscle after stimulation of the posterior tibial nerve at popliteal fossa.

If the H reflex was absent, the intensity of the stimulation was increased to supramaximal and F potential in the same muscle was determined. In normal subjects, the F wave latency (own values: 32±2.78 ms) was by 3 ms longer than the ipsilateral H reflex latency. A variety of facilitation techniques including handgrip and slight voluntary activity were attempted before concluding that the F wave and H reflex were absent.

Sensory nerve action potentials (SNAP) were recorded with surface electrodes from the median nerve at the wrist upon index stimulation through ring electrodes and behind the lateral malleolus upon sural nerve stimulation at lower leg. The latency to the beginning and the peak-to-peak amplitude of sensory potentials were measured.

Fig. 1. Changes in the maximum thenar M potential on stimulation at proximal sites of the nerve. Conduction block was demonstrable across the Erb-to-axilla segment.
In each patient, one-sided nerves were generally analyzed. Study nerves were selected on the basis of clinical data and results of needle electromyography. If both sides were tested, only data from the side with more severe electrophysiological abnormalities were considered.

The values of each variable were compared with the upper and lower limits of normal for our laboratory and also with abnormal values suggestive of demyelination. The mean ± 2 standard deviations was taken as the upper or lower limit of normal. Abnormal values suggestive of demyelination in nerve conduction studies were defined as follows:

- >125% of upper limit of normal in distal latency if the amplitude exceeded 80% of lower limit of normal;>
- 120% of upper limit of normal in F wave and H reflex latency if the amplitude exceeded 80% of lower limit of normal;
- <80% of lower limit of normal in motor and sensory conduction velocity if the amplitude exceeded 80% of lower limit of normal;
- >50% proximal-distal CMAP amplitude decrease in the absence of abnormal temporal dispersion for partial conduction block (CB).

Statistical analyses were performed by using χ²-test (for categorical variables) and Student’s t-test (for normally distributed continuous variables). Probabilities of less than 0.5 were considered significant. Only values suggestive of demyelination were statistically analyzed.

Results

There were 51 patients (32 male and 19 female), age range 20–79 (mean 50.5±15.22) years. The highest frequency of affection was in the sixth decade of life (31.4% of patients). According to the clinical and electrophysiological findings, 46 patients had acute inflammatory demyelinating polyradiculoneuropathy (AIDP), one patient had Miller Fisher syndrome, and four patients had axonal forms. Patients were classified as having axonal form of GBS if there was no electrophysiological evidence of demyelination at initial and follow up studies.

In all patients with axonal variety, early electrophysiological findings were similar: low distal CMAP amplitudes or unexcitable nerves, normal motor and sensory conduction velocities, normal distal latencies, F waves absent or of normal latency, and normal sensory neurography. The results of electrodiagnostic testing in AIDP patients are summarized in Table 1.

**H reflex and F wave**

Absent H reflex in soleus muscle was recorded in 90.7% of AIDP patients and it was the most common abnormal finding. The frequency of F wave latency prolongation in soleus muscle was similar to that in short extensor muscle of toe. In soleus muscle, prolonged F wave latency was recorded in 24 of 39 patients with absent H reflex in that muscle, and in nine of them prolongation was in demyelinating range.

**Conduction block**

CB in the Erb-to-axilla segment was observed in 22 (78.6%) of 28 patients; in 12 of them, CB was only present in the Erb-to-axilla segment. In only three of 28 patients there was no CB in any median and ulnar nerve segment.

In three of 28 patients, CB in the Erb-to-axilla segment was the only abnormality observed, along with absent H reflex. The amplitudes of CMAP evoked by stimulation at the wrist were analyzed in these 28 patients. A reduced distal CMAP amplitude (below 3 mV) was recorded in the abductor muscle of thumb in eight (28.6%) of 28 patients and in the abductor muscle of little finger in six (21.42%) of 28 patients. These amplitude reductions were not accompanied by prolonged CMAP duration.

Median nerve CB was significantly more common in the Erb-to-axilla segment than distal CMAP amplitude reduction (P=0.0004), and CB in the forearm (P=0.0004) and upper arm (P=0.0001) segments.

Ulnar nerve CB was significantly more common in the Erb-to-axilla segment than in the upper arm (P=0.0001), forearm (P=0.0001) and elbow (P=0.0029) segments.

**Motor conduction velocity**

When MCV was analyzed in individual median nerves, slow MCV was significantly more frequent in the Erb-to-axilla segment than in the upper arm (P=0.0054) and forearm (P=0.0001) segments. There was no significant difference between MCV slowing down in the Erb-to-axilla segment and prolongation of F wave latency (P=0.8101) (Fig. 2).
Slowing down of ulnar nerve MCV in the Erb-to-axilla segment was more frequent than in other segments but the difference was not significant. These different results in the frequency of slow MCV along ulnar and median nerve segments were probably the consequence of different numbers of patients analyzed.

In patients with early AIDP, the mean MCV was significantly ($P<0.01$) slower in all segments as compared with the control group of normal subjects; slow-
ing down was most pronounced in the most proximal segments (median nerve: Erb-to-axilla segment \( P = 0.0001 \); upper arm \( P = 0.009 \); forearm \( P = 0.0021 \); ulnar nerve: Erb-to-axilla segment \( P = 0.0001 \); upper arm \( P = 0.0011 \); elbow \( P = 0.0014 \); and forearm \( P = 0.047 \)) (Fig. 3).

Sensory neurography

In our series of early AIDP patients, 22 (48.9%) of 45 patients had normal sural nerve neurography and 14 (31.1%) of 45 had normal median nerve sensory neurography; the difference was not significant (\( P = 0.1315 \)).

Median nerve SNAPs were abnormal in 31 (68.9%) patients: sensory responses were absent in seven (15.6%) patients and of reduced amplitude in 24 (53.3%) patients.

Sural nerve SNAPs were abnormal in 23 (51.1%) patients: sensory responses were absent in nine (20.0%) patients and of reduced amplitude in 14 (31.1%) patients.

In eight (17.8%) of 45 patients, median nerve sensory neurography was abnormal with normal sural nerve neurography, whereas none of the patients showed abnormal sural nerve neurography with normal median nerve sensory neurography.

The reduction of sural and median nerve SNAP amplitudes was more frequent than sensory conduction slowing down, the difference being statistically significant for both sural and median nerves (\( P = 0.0001 \) both).

Discussion

Conduction block and conduction slowing are electrophysiological hallmarks of peripheral nerve demyelination. Experimental demyelination has shown that CB is an early manifestation of demyelination, whereas slow conduction velocity is a characteristic of remyelinating fibers\(^{13}\). Several authors conclude that CB is more frequently observed in the early stage of GBS, when it may be the only sign of demyelination and the main reason of acute paralysis in GBS\(^{14,15}\). In the present study, CB was also the most commonly observed abnormality. In all nervous segments, it was more frequently recorded than MCV slowing down. CB indirectly determined as absent H reflex was recorded in 90.7% of patients and as such it was the most common electrophysiological abnormality in our group of early GBS patients.

Most large GBS studies suggest that electrophysiological abnormalities may not be randomly distributed but rather are greater in terminal and most proximal segments of the peripheral nervous system and across common sites of entrapment\(^{5,14,16-20}\).

The reason for this distribution may be relative deficiency in the blood-nerve barrier in these regions\(^{20,21}\).

Some other authors have proposed that some patients have a more widespread distribution of involvement with sequential patchy areas of demyelination along the course of the motor nerve\(^{12,23}\).

The numerous demyelinated segments along the nerve cumulatively slow the conduction velocity down, which can be preserved early in the course of the disease.
Our results indicated the most proximal segment to be most frequently affected in early GBS. When the incidence of abnormalities was analyzed in individual nerves, CB and motor conduction slowing were more common in the Erb-to-axilla segment than in more distal segments. These results are in concordance with some previous reports. By direct MCV measurement in the nerve segment between spinal cord and axilla, Mills and Murphy conclude that proximal CB is the major abnormality in early GBS18.

In patients with chronic inflammatory demyelinating polyradiculoneuropathy, CB was usually detected in distal nerve segments, which makes electrophysiological difference between patients with AIDP and chronic inflammatory demyelinating polyradiculoneuropathy24.

Brown and Feasby also report on CB as the main electrophysiological abnormality in the first two weeks of acute GBS. They found no proximal predilection; in some nerves, CB was predominantly proximal, in others predominantly distal, and in some nerves CB was generalized in its distribution14.

In our series of patients, we confirmed the known tendency toward involvement of the common sites of nerve compression. CB was more frequently observed in the elbow and carpal tunnel segments than in the upper arm and forearm segments, however, the difference did not reach statistical significance.

Absent or prolonged F waves are common findings in AIDP19,25, and absent H reflex has been reported by several authors as the most common finding25-27. In our patients, we found a similar incidence of abnormalities in F waves and H reflex. Absent H reflex in isolation is present in most polyneuropathies, thus being a nondiagnostic category for AIDP27. Some more information can be provided by recording F waves in soleus muscle. In 23.8% of our patients with absent H reflex in soleus muscle, the prolonged F wave latency in the same muscle was indicative of demyelination. For that reason, we consider assessing both H reflex and F wave in soleus muscle very useful in diagnosing the condition.

In our series of early AIDP patients, abnormal sural nerve neurography was also more frequent than median nerve sensory neurography. The “sural-sparing pattern” in patients with AIDP is reported by other authors26,27.

Many experts do not accept stimulation at Erb’s point as being sufficiently reliable in producing supramaximal stimulation to be included in the criteria for definitive partial CB, but only for probable partial CB8. We consider that assessing proximal nerve segments by Erb’s point stimulation is a useful method in early confirmation of the diagnosis in many patients, especially those with inconclusive electrophysiological finding in distal nerve segments. It is true that greater care is necessary to ensure supramaximal stimulation at Erb’s point, but in patients with early GBS, very informative data can be obtained by assessing proximal nerve segment because electrophysiological abnormalities are here more frequent and more specific than in distal nerve segments.

References
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Sažetak

ELEKTROFIZILOŠKI NALAZI U RANOM GUILLAIN-BARRÉOVU SINDROMU

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Cilj studije bio je utvrditi najčešće elektrofiziološke nenormalnosti u ranom Guillain-Barréovu sindromu (GBS). Ispitani su neurofiziološki nalazi 51 bolesnika s GBS koji su pregledani unutar 12 dana od pojave simptoma. Akutna upalna demijelinizacijska poliradikuloneuropatija (AIDP) bila je prisutna u 46 od 51 bolesnika s GBS. U bolesnika s AIDP zabilježene su slijedeće nenormalnosti: odsutan H refleks u 90,7%, blokada provodljivosti u segmentu Erb do aksile u 78,5%, brzina motorne provodljivosti koja ukazuje na demijelinizaciju u segmentu Erb do aksile u 45,2%, produžena latencija F vala u 65,2%-73,8%, ali samo 20,0%-37,0% s produženom latencijom F vala koja ukazuje na demijelinizaciju, te smanjen ili odsutan akcijski potencijal senzornih živaca u 62% bolesnika. Nenormalne vrijednosti terminalnih latencija te motorne i senzorne brzine provodljivosti u distalnim segmentima živaca koje ukazuju na demijelinizaciju zabilježene su u manje od 30% bolesnika. Zaključuje se kako je blokada provodljivosti u najproksimalnijim segmentima perifernog živčanog sustava, koja se određuje izravno u segmentu Erb do aksile ili neizravno kao odsutan H refleks, najosjetljiviji parametar u bolesnika s ranim GBS. Ispitivanja motorne provodljivosti u segmentu Erb do aksila pružaju korisne informacije kod bolesnika s ranim GBS.

Ključne riječi: Guillain-Barréov sindrom; Živčana provodljivost; Elektromiografija