ADMISSION NEUROPHYSIOLOGICAL ABNORMALITIES IN GUILLAN-BARRE' SYNDROME: A SINGLE-CENTER EXPERIENCE.

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Introduction: Guillain-Barré syndrome (GBS) is most commonly a post-infectious disorder that usually occurs in otherwise healthy people. The main features of GBS are rapidly progressive bilateral and relatively symmetric weakness of the limbs with or without involvement of respiratory muscles or cranial nerve-innervated muscles.
It has been demonstrated that an early diagnosis reduces the morbidity and improves the prognosis of the disease. However, the diagnosis can be difficult in the early phases of the disease. Clinical symptoms may be poorly specific and the onset of the albumin-cytologic dissociation in cerebrospinal fluid is often delayed.
The results of nerve conduction studies (NCS) are therefore crucial for early identification of GBS patients. For this reason neurophysiological criteria for GBS diagnosis have been proposed. However the reliability of these criteria early in the course of GBS has not been yet well established. Indeed few studies have been focused on the neurophysiological abnormalities in early GBS. Generally these studies concluded that the earliest and most reliable neurophysiological abnormalities were abnormal H reflexes, F waves latencies, and increased distal motor latencies. On the other hand these reports often included few patients examined at different time intervals.

Patients and Methods: We retrospectively reviewed the medical records and NCS of all GBS patients investigated in our Neurology department in an 14 years interval (1999-2013). We included patients in whom the clinical history, laboratory tests and NCS suggested GBS and not another disease. Patients had to display a progressive weakness in both arms and legs with absent/reduced reflexes, associated or not with sensitive deficiency and/or autonomic dysfunction. All patients reached a nadir by 4 weeks. The disease had to be monophasic so as to exclude chronic inflammatory demyelinating polyneuropathy. NCS had to be performed within two weeks after onset of symptoms. Modified Rankin scale was used to assess clinical severity.
We excluded patients with a previously known polyneuropathy or with a predisposing condition such as diabetes, alcoholism, chronic kidney disease and exposition to neurotoxic drugs. We also excluded patients with Miller–Fisher syndrome.
We further divided our cohort in three subgroups according to the interval from symptoms onset to NCS (≤ 4 days; 5-7 days; 8-14 days).
Motor and sensory NCS were performed using standard techniques, as previously described. All studies were performed in a warm room and skin temperature was >32°C; if needed, an infrared lamp was used to warm the studied segment. Distal motor latency (DML) was measured at the onset of compound muscle action potential (CMAP). We considered all the examined segments for evaluation of conduction block (CB), defined as a reduction greater than 50% of the proximal CMAP amplitude and area compared to the distal CMAP. CB was assessed only in nerves with distal CMAP amplitude of at least 1 mV.

Patients results:

- Whole cohort: seventy one GBS patients underwent NCS in our department within two weeks from symptom onset in the period examined (1999-2013). Age at onset from 19 to 83 years (mean 53.73, median 55, SD±16.11). Ratio of men to women was 1.73:1 (45/26). Mean Rankin scale 3.79 (range 1-5; median 4; DS±0.97). A previous infection reported in 41 cases.

- First group (NCS performed within 4 days from onset): 24 patients. Age at onset from 19 to 83 years (mean 52.08, median 51.5, SD±18.00). Ratio of men to women 1.18:1 (13/11). Mean Rankin scale 3.5 (range 1-5; median 4; DS±1.06). A previous infection reported in 14 cases.

- Second group (NCS performed within 5-7 days from onset): 18 patients. Age at onset from 21 to 73 years (mean 50.33, median 51.5, SD±14.76). Ratio of men to women 5:1 (15/3). Mean Rankin scale 3.83 (range 2-5; median 4; DS±1.10). A previous infection reported in 14 cases.

- Third group (NCS performed within 8-14 days from onset): 29 patients. Age at onset from 31 to 79 years (mean 57.20, median 63, SD±15.11). Ratio of men to women 1.41:1 (17/12). Mean Rankin scale 4 (range 3-5; median 4; DS±0.76). A previous infection reported in 13 cases.

Nerve conduction studies results:

Detailed frequency of each abnormal parameter for single groups are summarized in Figure 1.

The main abnormality were absent or prolonged F waves from lower limbs, found overall in 63% of patients with ≤ 4 days evaluation, in 83% with 5-7 days examination, and in 97% with 8-14 examination.
The other abnormalities were not so frequent (<50% of cases) in the early examinations, being the most present abnormal F wave in upper limbs, and they proportionally increased with the time from the onset.
A great proportion of patients with an early NCS evaluation (37%) showed normal results. The percentage of normal NCS in first group was significantly higher if compared with the percentage found in the other two groups (p =0.0126 and p =0.0002, respectively. Fisher's test).
Conduction blocks were more often observed in upper limbs and their occurrence was similar in the three groups (about 30%).
Sensory NCS of the upper limbs resulted more often abnormal if compared with those of the sural nerves. The frequency of abnormal sensory NCS in upper limbs increased with the interval of the examination from symptoms onset, while the frequency of abnormal NCS of sural nerve was substantially unchanged.

No significant differences were observed in clinical severity ($p > 0.05$) among the three groups, nor between all patients with normal NCS and patients of first group (Figure 2). Conversely, mean Rankin of all patients with normal NCS was less severe than those of the entire group ($p = 0.0032$) and when compared with those of patient from second ($p = 0.0187$) and third ($p = 0.0002$) group (Figure 2).

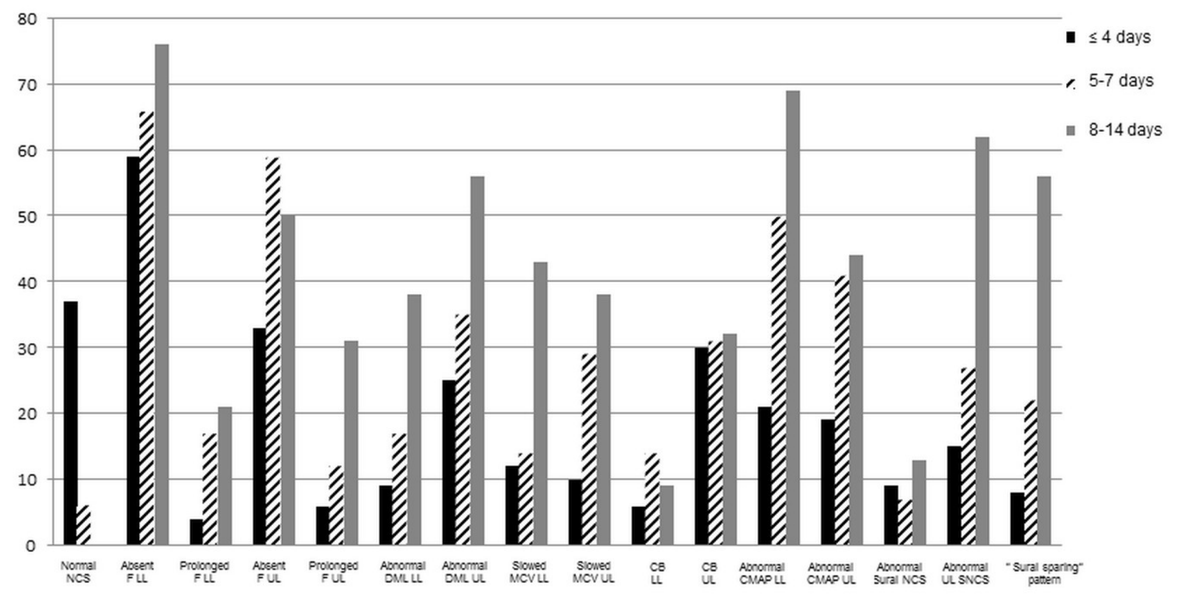

Figure 1. Histogram of % abnormalities for each parameters of nerve conduction studies (NCS). F, F wave mean latency; LL, lower limbs; UL, upper limbs; DML, distal motor latency; MCV, motor conduction velocity; CB, conduction blocks; CMAP, compound muscle action potential; SNCS, sensory nerve conduction studies.

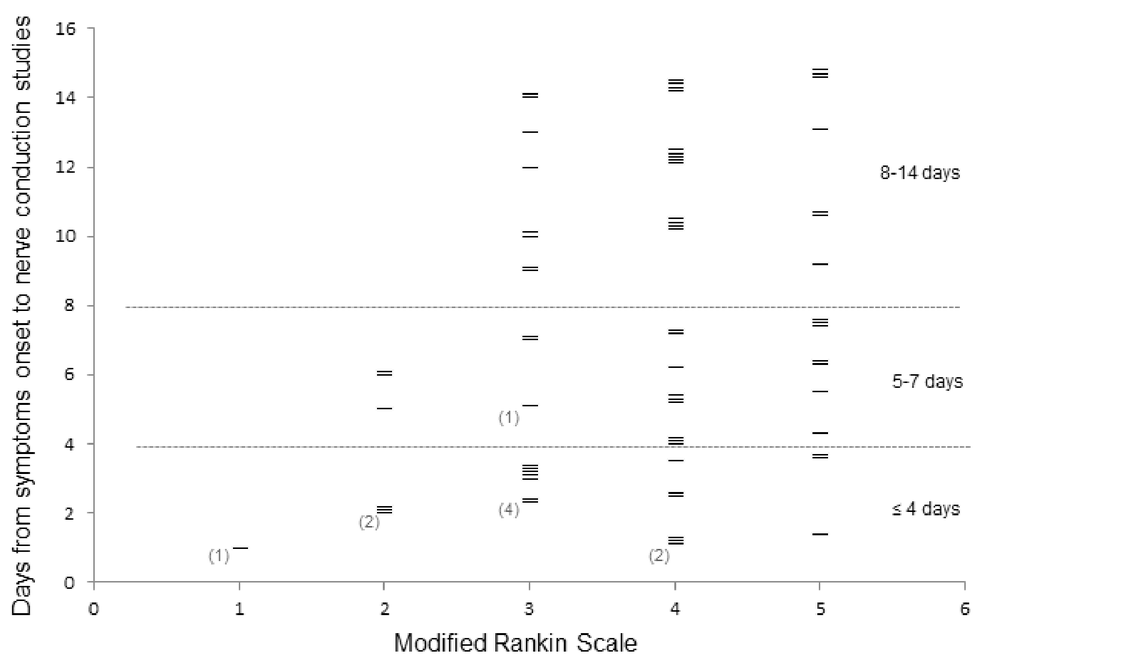

Figure 2. Distribution of patients according to time from symptoms onset to neurophysiological examination (days) and clinical severity (Modified Rankin Scale). Numbers in brackets indicate patients with normal nerve conduction studies (NCS). No significant differences were observed in clinical severity ($p > 0.05$) among the three groups (≤ 4 days; 5-7 days; 8-14 days), nor between all patients with normal NCS and patients with early neurophysiological examination. Conversely, mean Rankin of all patients with normal NCS was less severe than those of the entire group ($p = 0.0032$) and when compared with those of patient with 5-7 days examination ($p = 0.0187$) and with 8-14 days examination ($p = 0.0002$).

Conclusions:

-Abnormal F wave (absent or prolonged) was the most frequent abnormality detected, especially in lower limbs. The frequency of this abnormality increased with the time of examination from onset. This result was similar to previous studies.
-Other abnormalities (including demyelinating alterations) were not so frequent in the early evaluations and, obviously, they increased with the time.
-Conduction blocks were detected in about a third of patients, especially in upper limbs, and their frequency did not increase with the time between symptoms onset and NCS. In view of this data we suggest to always examine also upper nerve limbs when GBS is suspected.
-Sural nerve resulted normal in a great proportion of patients, also in those with a late examination. Conversely NCS of sensory upper limbs nerves were generally abnormal, especially in patients with a late examination. The combination of the two results confirms that the "sural sparing" pattern (abnormal sensitive upper limbs nerves studies associated with normal sural nerves sensitive studies when sensitive symptoms are present in the lower limbs) is typical for GBS syndrome.
-High percentage of patients (37%) with an early examination (≤ 4 days) showed normal NCS. Our results confirm that a normal NCS do not exclude a clinical diagnosis of GBS.

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