Early Electrodiagnostic Findings in Guillain-Barré Syndrome

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Context: Guillain-Barré syndrome (GBS) is the foremost cause of acute, generalized, peripheral neuropathic weakness. Although nerve conduction studies are a diagnostic aid, the characteristic electrical changes may not evolve for several weeks. Early diagnosis of GBS is important, however, because early treatment has been shown to improve outcome.

Objectives: To describe the electrodiagnostic abnormalities detectable in the first week of GBS, to determine if there are early patterns suggestive of GBS, and to identify the percentage of patients whose condition can be diagnosed with reasonable certainty in the first week.

Design and Setting: We retrospectively reviewed the medical records of all patients admitted to the Cleveland Clinic Foundation, Cleveland, Ohio, having the discharge diagnosis GBS during the past 16 years. Patients who underwent nerve conduction studies within 7 days of muscle weakness were selected for this study.

Results: The H reflex was absent in 30 (97%) of 31 patients. Nineteen patients (61%) had low-amplitude or absent sensory nerve action potential (SNAP) in the upper extremity. Fifteen patients (48%) overall, including 21 (67%) of the 31 patients, including 14 (67%) of the 21 patients younger than 60 years, had an abnormal upper extremity SNAP combined with a normal sural SNAP. Other findings included an abnormal F wave (25 patients [84%]), reduced compound muscle action potential amplitude (22 patients [71%]), prolonged distal latency (20 patients [65%]), temporal dispersion (18 patients [58%]), slowed motor conduction velocity (16 patients [52%]), and motor conduction block (4 patients [13%]). Definite diagnosis was possible in 17 patients (55%), but not commonly until the fifth day.

Conclusions: The H reflex is the most sensitive test for early GBS. Upper extremity SNAPs are also frequently abnormal in early GBS. Absent H response, abnormal F wave, and abnormal upper extremity SNAP combined with a normal sural SNAP are characteristic of early GBS. If multiple nerves are tested, definite diagnosis is possible in half the patients, but not until the fifth day after the onset of symptoms.

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Guillain-Barré syndrome (GBS) is the most common cause of acute and severe generalized peripheral neuropathic weakness. Nerve conduction studies (NCSs) are the most important ancillary diagnostic test. Electrodiagnostic (EDX) studies often show evidence of patchy demyelination, manifested as conduction block, slowed motor conduction velocities (CVs), delayed latencies, and dispersed responses; however, axon loss variants have been described. While the electrical abnormalities may not be sufficiently widespread for definite diagnosis in the first 2 weeks, early diagnosis is important, because treatment shortens the course of GBS, reduces the time required to receive mechanical respiratory assistance, and lessens the overall severity. The goal of this study was to determine if there are characteristic EDX findings within the first week or if there are early patterns that are suggestive of GBS so that interventional treatment may be initiated with confidence. We retrospectively reviewed the medical records of all patients with GBS who underwent EDX studies at our center within the first 7 days after onset of motor symptoms to determine the most common early electrical findings and the percentage of patients who could be diagnosed with reasonable certainty.

RESULTS

CLINICAL DATA

Of the 31 patients (20 males and 11 females) who ranged in age between 4 and 76 years (mean age, 50 years), 21 were younger than 60 years (Table 1). Twenty-two patients (71%) had an infection or surgery in the prior month. At hospital admission, all had motor weakness; 29 (94%), loss of deep tendon reflexes; 1 (0.3%), reflexes present only with reinforcement; and 3 (10%), acute sensory loss. One patient was diagnosed as
PATIENTS, MATERIALS, AND METHODS

SELECTION OF PATIENTS

We retrospectively reviewed the medical records of all patients given the clinical diagnosis of GBS during the past 16 years. Those patients who underwent EDX testing within 7 days after the onset of motor symptoms were selected for this study. Patients were included if findings from the clinical, radiographic imaging, laboratory, and EDX studies combined were suggestive of GBS and not another disorder. Inclusionary criteria for the clinical diagnosis of GBS were rapidly progressive limb weakness with or without distal limb paresthesias and reduced deep tendon reflexes. One patient with ataxia, ophthalmoplegia, and areflexia was diagnosed as having the Miller-Fisher syndrome. Patients with autonomic instability and respiratory failure in addition to the aforementioned symptoms were also included in this study. Excluded from the study were patients with other causes of nerve conduction abnormalities (eg, renal failure or diabetes mellitus) and patients with evidence of another neuromuscular diagnosis (eg, myelopathy, familial polyneuropathy, multiple mononeuropathies, or chronic peripheral polyneuropathy).

LABORATORY STUDIES

Serum chemistry levels, complete blood cell count, and heavy metal screening results were recorded. In addition, most patients underwent lumbar puncture and analysis of cerebrospinal fluid. Twenty-seven patients (87%) had their cerebrospinal fluid studied within the first week after the onset of motor symptoms.

EDX STUDIES

Motor NCS were performed in an ipsilateral upper extremity (UE) and lower extremity (LE) using surface electrodes. Skin temperature was above 32°C in all patients. When abnormal results were obtained, often some motor NCSs were performed in the contralateral limb for comparison. Sensory NCSs were performed, using antidromic techniques, on the median nerve, ulnar nerve, superficial radial nerve, and sural nerve. Motor NCSs included stimulation of the median and ulnar nerves at the wrist and forearm while recording from the abductor pollicis brevis muscle and abductor digiti minimi muscle of the hand, respectively, and of the deep peroneal and posterior tibial nerves at the ankle and knee, while recording from the extensor digitorum brevis muscle and the abductor hallucis muscle, respectively. Supraclavicular stimulation was performed on one or more UE motor nerves, usually the ulnar nerve, in an attempt to identify conduction block or slowing proximal to the elbow. F waves were measured with each motor NCS for which a compound muscle action potential (CMAP) result was obtained. The H reflex was recorded from the gastrocnemius and soleus muscles after stimulation of the posterior tibial nerve. The CMAP amplitude, distal motor latency, motor nerve CVs, sensory nerve amplitude and peak latency, H reflex amplitude and latency, and shortest F response latencies were measured. A value was defined as abnormal if it fell outside the laboratory’s range of normal responses, which were corrected for age. Patients were classified as having polyradiculoneuropathy consistent with GBS if there was a combination prolonged distal motor latency (>150% of the upper limit of normal), CV slowing (<70% of the lower limit of normal), prolongation of F wave latency (>150% of the upper limit of normal), low CMAP amplitude or proximal CMAP drop suggestive of conduction block, or abnormal temporal dispersion in 2 or more nerves. Needle electrode examination (NEE) was performed in only some of the patients because of the proximity between the time EDX studies were performed and the point of symptom onset. In those patients in whom an NEE was performed, multiple muscles in the UE and LE were recorded.

Sensory Nerve Action Potentials

One or more SNAPs were absent in the UE in 12 patients (39%), of low amplitude in 6 patients (19%), and

F Waves

Some abnormality of F waves (prolonged latency or absent response) was detected in 26 patients (84%). The UEF waves were absent in 1 or more nerves in 17 patients (55%), of prolonged latency in 6 patients (19%), and normal in 8 patients (26%). The LEF waves were absent in 1 or more nerves in 19 patients (61%), of prolonged latency in 4 patients (13%), and normal in 8 patients (26%). While most patients had absent F waves, none met strict criteria for demyelination with latency prolongation greater than 130% of the upper limit of normal. Eighteen patients (58%) had at least 1 motor nerve with a normal F wave response. Six patients (19%) had only a single abnormal F wave. Five patients (16%) had completely normal F wave findings of at least 2 nerves in each limb. No patient had only abnormal F waves without other NCS abnormalities.

EDX DATA

H Waves

The H reflex was absent in 30 (97%) of 31 patients (Table 2). It was of low amplitude in the single remaining patient, and it was absent in all 21 patients younger than 60 years. It was absent in the only patient with Miller-Fisher syndrome. The EDX study findings were completely normal, with the exception of absent H waves in 5 patients (16%).
delayed in 1 patient (ulnar nerve). Overall, 19 patients (61%) had 1 or more abnormal UE SNAPs. The abnormalities affected all nerves in the UE without predilection for a single nerve. The sural SNAP was normal in 26 patients (84%), including 19 (90%) of 21 patients younger than 60 years in whom this response is routinely seen. The combination responses of an absent UE SNAP and a normal sural SNAP were seen in 9 patients (29%), 8 (38%) of whom were younger than 60 years. There was a combined response of an absent or low-amplitude UE SNAP and a normal sural SNAP in 19 (67%) of the 31 patients younger than 60 years. Viewed from a different perspective, in patients with a normal sural response, 15 (58%) had an abnormal SNAP in the UE, including 14 (74%) younger than 60 years, who had reduced amplitude (n=2 patients), delayed latency (n=1 patient), unelicitable response (n=1 patient), or some combination thereof (n=10 patients).

Motor NCS

Abnormalities of CMAP involved both the UE and LE, often in combination, without predilection for a particular nerve. Twenty-two patients (71%) had reduced CMAP amplitude of at least 1 nerve with distal stimulation. The amplitude was reduced in only 1 nerve in 3 patients and in more than 1 nerve in 19 (61%). Responses were absent in 1 or more nerves in 2 patients. Five patients were shown to have significant axon loss on follow-up NEE.

Distal Latency

The distal latency (DL) was prolonged in at least 1 nerve in 20 patients (65%), in just 1 nerve in 6 patients (19%), and in multiple nerves in 14 patients (45%). Thirteen (65%) of the 20 patients had DLs exceeding 150% of the upper limit of normal. The prolongation was detected in the UE and LE equally.
patients (48%). Overall, 18 patients (58%) had CMAP dispersion in at least 1 nerve.

**ELECTROMYOGRAPHIC FINDINGS**

Needle electrode examination was performed in only 6 patients because of the proximity of EDX assessment to symptom onset. Motor unit potential number and recruitment was reduced in all patients. One patient had fibrillation potentials in proximal UE and LE muscles on initial NEE just 5 days after the onset of motor symptoms.

Definite diagnosis of GBS was possible because of some combination of motor CV slowing, reduction of CMAP amplitudes, abnormal dispersion, conduction block, or prolongation of minimum F wave latency in 2 or more nerves in 17 patients (55%). The H reflex was the only frequently abnormal finding from the onset of symptoms. The constellation of findings necessary for definite diagnosis was not commonly seen until the fifth day (Table 3).

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**COMMENT**

To our knowledge, no EDX trial has been concerned solely with patients whose GBS symptoms were of 1 week or less. The purpose of this study was to identify the most common early EDX abnormalities found with GBS. Diagnosis within the first week is often difficult because the elevation of the cerebrospinal fluid protein level and motor NCS changes may not evolve until later, yet early diagnosis is desired, since several treatments have been shown to lessen the disease severity and improve outcome. We assessed 31 patients who underwent EDX testing within 7 days of onset of motor weakness. We identified the earliest EDX changes and the percentage of patients whose diagnosis could be made with certainty. Definite diagnosis was based on a constellation of findings including slowed motor CV, delayed latencies, dispersion of responses and conduction block, low distal CMAP amplitudes, and prolongation of minimum F wave latency. We chose the timing of disease onset to be the appearance of clinical weakness because that symptom is most readily identifiable. Motor symptoms may not definitely represent commencement of disease in all patients, however.

Electrodiagnostic studies have been used in the diagnosis of GBS for almost 50 years. Initial EDX investigations showed multifocal demyelination to be a common underlying pathophysiological condition. Large studies have included patients with symptoms for less than 1 week, although H reflexes and sensory NCS abnormalities in this group specifically were not commented on. In the report by Ropper et al, 41 patients underwent EDX studies within 1 week of symptom onset. Sixteen of these patients had multiple abnormalities of CMAPs, including dispersion, delayed latency, low amplitude, CV slowing, conduction block, or abnormal F waves. Only 5 of these patients, however, had CV slowing of less than 80% of the lower limit of normal in at least 2 nerves. Fifteen had some abnormality of F wave. Clouston et al assessed the CMAP in 47 patients with GBS, 20 of whom were evaluated less than 1 week from symptom onset. Thirteen had at least 1 nerve with low-amplitude CMAP; in 10 of these patients the CMAP amplitude fell with proximal stimulation suggesting conduction block. Those patients with low-amplitude CMAPs had a poorer outcome.

An axon loss variant of GBS, termed “acute axonal motor neuropathy” or “acute motor and sensory axonal neuropathy” occurs in 11% of these patients and is associated with slower recovery. Occasionally, primary demyelination with secondary axonal damage will mimic clinically and electrophysiologically the axonal variant of GBS. However, in addition, a syndrome of rapidly progressive and severe but reversible weakness with low CMAP amplitude has been identified in Chinese children. The reduced CMAP amplitude in some of these children represents severe distal demyelination with variable axon loss. Hence, severe reduction in CMAP amplitude early in the course of GBS may be caused by distal demyelination, axon loss, or both, and so inexactly reflects prognosis. Five of the 20 patients in our study with low CMAP amplitudes may have had distal conduction block, although there was no definite proof.

Diagnostic criteria for the early detection of GBS, when EDX changes are not yet fully apparent, have been proposed but have focused largely on motor NCS and have not included the H reflex or the comparison of the results of the different sensory studies. The H reflex is a sensitive objective test for detecting subtle abnormalities of the S1 nerve root and for detecting early polyneuropathy. While correlation with presence of the Achilles reflex is high, it is not absolute and interexaminer variability has been reported in testing the ankle jerk. Our data show that the H reflex test is the most sensitive test for early GBS. The H

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Table 3. Evolution of Nerve Conductive Study (NCS) Changes

<table>
<thead>
<tr>
<th>Change†</th>
<th>Day 1 to 4 (n = 8)</th>
<th>Day 5 to 7 (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent H reflex</td>
<td>7 (88)</td>
<td>23 (100)</td>
</tr>
<tr>
<td>Normal NCS (except H reflex)</td>
<td>3 (38)</td>
<td>2 (9)</td>
</tr>
<tr>
<td>F-Waves</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal‡</td>
<td>6 (75)</td>
<td>20 (87)</td>
</tr>
<tr>
<td>Absent</td>
<td>4 (50)</td>
<td>17 (74)</td>
</tr>
<tr>
<td>Prolonged</td>
<td>2 (25)</td>
<td>3 (13)</td>
</tr>
<tr>
<td>Normal</td>
<td>2 (25)</td>
<td>3 (13)</td>
</tr>
<tr>
<td>SNAP response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal UE‡</td>
<td>2 (26)</td>
<td>17 (73)</td>
</tr>
<tr>
<td>Absent UE</td>
<td>1 (13)</td>
<td>11 (48)</td>
</tr>
<tr>
<td>Abnormal UE/normal sural SNAP</td>
<td>2 (25)</td>
<td>13 (57)</td>
</tr>
<tr>
<td>Absent UE/normal sural SNAP</td>
<td>1 (13)</td>
<td>8 (35)</td>
</tr>
<tr>
<td>CMAP response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low amplitude‡</td>
<td>3 (38)</td>
<td>19 (83)</td>
</tr>
<tr>
<td>≥2 Nerves</td>
<td>3 (38)</td>
<td>16 (70)</td>
</tr>
<tr>
<td>Prolonged latency‡</td>
<td>2 (25)</td>
<td>18 (78)</td>
</tr>
<tr>
<td>≥2 Nerves</td>
<td>1 (13)</td>
<td>13 (57)</td>
</tr>
<tr>
<td>Slow velocity CV‡</td>
<td>2 (25)</td>
<td>14 (61)</td>
</tr>
<tr>
<td>≥2 Nerves</td>
<td>1 (13)</td>
<td>12 (52)</td>
</tr>
<tr>
<td>Proximal conduction block‡</td>
<td>1 (13)</td>
<td>3 (13)</td>
</tr>
<tr>
<td>Temporal dispersion‡</td>
<td>3 (38)</td>
<td>15 (65)</td>
</tr>
</tbody>
</table>

* Data are given as number (percentage) of patients.
† SNAP indicates sensory nerve action potential; UE, upper extremity; CMAP, compound muscle action potential; and CV conduction velocity.
‡ Number of patients with 1 or more abnormal study findings.
reflex was absent or abnormal in all of our patients from symptom onset (Table 2), including all 21 patients younger than 60 years in whom it is normally obtainable. It was abnormal earlier and more often than other procedures, which were not commonly abnormal until day 5 and it was the sole abnormality in 5 (16%) of our 31 patients. It was unobtainable in the patient who had Miller-Fisher syndrome. In this regard, the H reflex test was more sensitive than F wave studies. Eighteen (58%) of our 31 patients had at least 1 normal F wave study, and often multiple nerves had to be tested to detect F wave abnormality. Our experience suggests that H reflex assessment should become part of the standard repertoire in the early diagnosis of GBS. Nevertheless, unobtainable H waves, similar to unobtainable F waves, are nonspecific and nondiagnostic by themselves because they are not conclusive evidence of demyelination.

Sensory nerve action potentials are also frequently abnormal in early GBS. Vague sensory symptoms precede motor weakness by hours to weeks in many cases. We identified the unusual combination of normal SNAPs in the LE (usually the sural nerve) and low-amplitude or absent SNAPs in the UE in almost half of our 31 patients. This percentage increased to two thirds in our patients younger than 60 years, in whom a sural SNAP would normally be present. Although there is nothing abnormal about a normal sural NCS response, and nothing diagnostic regarding a low-amplitude UE SNAP, this combination of changes should be considered indicative of an acquired demyelination disorder, especially when seen with an absent H reflex. These findings together are almost never seen in other polyneuropathies, except chronic inflammatory demyelinating polyneuropathy, or with other disorders that mimic GBS.

Finally, our data show that findings sufficient for diagnosis are more common after the fourth day from motor symptom onset (Table 3), are not necessarily suggestive of demyelination unless combined, and, as others have reported, are more likely to be discovered if multiple nerves are studied. While study findings other than the H reflex were frequently abnormal, including F waves (26 patients [84%]), CMAP amplitude (22 patients [71%]), DL (20 patients [65%]), motor CV (16 patients [52%]), or waveform (18 patients [58%]), these findings were patchy and were not commonly present until after the fourth day. There was no tendency for these abnormalities to occur in a specific nerve. Unlike the H wave, often multiple nerves had to be tested to detect a single abnormality and most patients had 1 or more normal F waves. Only 3 patients had motor CV slowing in our laboratory’s demyelinating range, thus, when present, motor CV slowing found within the first week was usually mild. This finding is worth emphasizing because significant CV slowing is often considered to be a hallmark of early GBS. Electrodiagnostic studies performed before the fifth day were likely to be nondiagnostic. In the patients for whom no definite EDX diagnosis was possible and in patients with symptoms of less than 4 days, the findings were usually nonspecific and not necessarily suggestive of demyelination even when combined. The diagnosis of GBS within the first week of motor onset is difficult, and in this sense, EDX studies are least helpful when they are most important. Certain EDX findings, especially absent H reflexes, abnormal F waves, and the combination of abnormal UE SNAP and a normal sural SNAP, while not suggestive of demyelination by themselves, are characteristic of acquired demyelinating polyradiculoneuropathies when they occur together. A constellation of abnormalities sufficient for definite diagnosis is more common after the fourth day from onset of motor weakness, is present in half of the patients, and is more easily detected if multiple nerves in several limbs are studied.

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