Guillain-Barré Syndrome: Clinicopathological Types and Electrophysiological Diagnosis

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ABSTRACT

Guillain-Barré syndrome had originally been described as an illness characterised by motor weakness, areflexia and albuminocytological dissociation in the cerebrospinal fluid. Subsequent reports have highlighted several variants of the syndrome with different clinical features and electrophysiological characteristics. In light of these studies, Guillain-Barré syndrome is best defined as encompassing a heterogeneous spectrum of clinicopathological entities. This article discusses different clinicopathological types of Guillain-Barré syndrome and their electrodiagnostic features.

Keywords: clinicopathological types, electrophysiology, Guillain-Barré syndrome

INTRODUCTION

In 1916, Guillain, Barré and Strohl described two patients with motor weakness, areflexia, and "albuminocytological dissociation" in the cerebrospinal fluid. This entity was later named Guillain-Barré syndrome (GBS). Subsequently, laid down diagnostic criteria also defined GBS as an illness typically characterised by progressive and symmetrical weakness of more than one limb with areflexia.[1] However, several variants of the syndrome with different clinical manifestations have been subsequently reported. GBS is best defined today as an illness encompassing a heterogeneous group of clinical and pathological entities. The clinical features and electrophysiological characteristics vary among different types and variants of the syndrome.

CLINICAL FEATURES

There are some features common to all types of GBS. Symptoms are preceded by an antecedent event in about two-thirds of patients.[2] Respiratory infections are the most commonly reported events in about 40% of patients within 1 month before the onset of GBS, followed by gastroenteritis in about 20% of cases.[2,3] Isolated case reports and some epidemiological studies have raised the possibility of vaccination as an antecedent event. However, a definite cause-effect relationship had only been demonstrated in the New Jersey influenza ("swine flu") vaccine and GBS during the 1976 to 1977 vaccination programme in the US.[4]

The onset of symptoms can be either acute or subacute. Gradual recovery occurs after a plateau phase. In a large study, the mean time to reach nadir, improvement, and clinical recovery were 12, 28, and 200 days, respectively. It has also been shown that 98% would reach the plateau phase by 4 weeks from onset.[3] Progressive signs and symptoms are seen in more than one limb, and are usually symmetrical in distribution.[1] Cranial nerve involvement and sensory signs vary among different types. Tendon reflexes are usually diminished or absent, but could also be preserved or even exaggerated in certain types which will be discussed later in this paper.

CLINICOPATHOLOGICAL TYPES

Acute Inflammatory Demyelinating Polyradiculoneuropathy

Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is the most common type of GBS, which would also fit into the original description of the syndrome. The most frequent manifestation is limb weakness, which can be more proximal than distal. Facial palsy is the most common cranial nerve involvement. Necropsy studies in AIDP have shown lymphocytic infiltration of the peripheral nerves and macrophage mediated segmental demyelination.[5] Axonal degeneration may occur as a secondary event. Clinical recovery is associated with subsequent remyelination.

Acute Motor Axonal Neuropathy

Acute motor axonal neuropathy (AMAN) was reported during the summer epidemics of GBS in 1991 and 1992 in northern China and 55 to 65% of patients with GBS belonged to this category.[6] However, in sporadic cases of GBS, only about 10 to 20% are of AMAN type.[7] Selective degeneration of motor axons is the pathological hallmark of this group. Clinically, this entity is characterised by rapidly progressing weakness which is often associated with respiratory failure, although patients usually have good recovery.[8] Tendon reflexes may be preserved or exaggerated.

Acute Motor Sensory Axonal Neuropathy

Studies from northern China identified another group of patients with a severe form of GBS, named acute motor sensory axonal neuropathy (AMSAN) based on their clinical, pathological, and electrophysiological characteristics.[5] These patients tended to have a fulminant course with slow and incomplete recovery. Necropsy studies have demonstrated Wallerian-like degeneration of sensory and motor fibres with little demyelination. This entity probably represents the most severe form of axonal damage in GBS.

Miller Fisher Syndrome

Miller Fisher syndrome is characterised by the triad of ataxia, areflexia and ophthalmoplegia. Mild limb weakness, ptosis, facial palsy, and bulbar palsy may also occur in some patients. Almost all demonstrate IgG autoantibodies against ganglioside GQ1b.[9] Immune mediated damage seems to occur in the paranodal regions of cranial nerves third, fourth, sixth and in the dorsal root ganglia.[9]

Sensory Guillain-Barré Syndrome

The possibility of a pure sensory variant of GBS has been raised by some authors. Oh *et al* reported 8 cases of acute demyelinating sensory neuropathy who met the following diagnostic criteria: acute onset symmetrical sensory loss; progression up to 4 weeks; diminished or absent reflexes; normal muscle power; electrophysiological evidence of demyelination in at least 2 nerves; monophasic course; no alternative cause for neuropathy; no family history of neuropathy; and in some, elevated cerebrospinal fluid protein.[10] This report cleared doubts on the existence of sensory Guillain-Barré syndrome.

A recent report describes another variant of sensory GBS identified as acute small fibre sensory neuropathy (ASFSN). These cases are characterised by acute onset numbness associated with burning dysaesthesia, normal muscle strength, symmetrical 'glove and stocking' type sensory loss for pain and temperature, normal proprioception and vibration senses and normal or brisk tendon reflexes. Selective involvement of small calibre sensory fibres is postulated in this entity, which seems to carry a favourable prognosis.[11]

Other Variants

Other variants of Guillain-Barré syndrome include pure dysautonomic, pharyngeal-brachial-cervical, ptosis without ophthalmoplegia, and paraparetic types.

ELECTROPHYSIOLOGICAL DIAGNOSIS

Diagnostic criteria for GBS has been formulated on clinical, laboratory, and electrophysiological parameters.[1] Early diagnosis is important in order to commence immunomodulatory therapy. Cerebrospinal fluid protein level may be normal during the first week, which makes electrophysiology the most useful tool for early diagnosis. Widespread electrophysiological abnormalities may not be recordable during the early phase. Nevertheless, there are certain electrophysiological features which would help confirm the diagnosis in the first week of illness. H-reflex appears to be the most sensitive test for early diagnosis. It has been shown that 97% have absent H-reflex while the remaining 3% have low amplitude H-reflex with normal latencies in the first week of GBS.[12] Other useful electrodiagnostic features during the early phase are abnormal F-waves (absent or prolonged latency), low amplitude compound muscle action potentials and prolonged distal latencies. These changes usually become evident after the fourth day of illness and are more likely to be detected if several nerves are tested.[12]

Acute Inflammatory Demyelinating Polyradiculoneuropathy

Segmental demyelination is the pathological hallmark in AIDP, which is reflected in electrophysiological findings. Electrodiagnosis of demyelination is primarily based on 4 parameters: conduction velocity; distal latency; temporal dispersion; and F-wave latency. The sets of diagnostic criteria vary slightly among different authors (Table 1).

Table 1. Electrodiagnostic criteria for demyelination of peripheral nerves.

Asbury *et al* [1]	Ho *et al* [6]	Hadden *et al* [17]
1. Reduction in CV in 2 or more motor. nerves.	Reduction of motor CV	Reduction of motor CV
(a) CV<80% of LLN if amplitude >80% LLN	(a) CV<90% of LLN if amplitude is >50% of LLN	(a) CV <90% of LLN
(b) <70% of LLN if amplitude <80% of LLN	(b) <85% of LLN if dCMAP is <50% of LLN	(b) <85% of LLN if amplitude is <50% of LLN
2. Prolonged distal latencies in two or more nerves	Prolonged distal motor latency	Prolonged distal motor latency
(a) DML >125% of ULN if amplitude is >80% of LLN	(a) DML >110% of ULN if amplitude is normal	(a) DML >110% of ULN
(b) >150% of ULN if amplitude <80% LLN	(b) >120% of ULN if amplitude is less than LLN	(b) >120% of ULN if dCMAP is <100% of LLN
3. CB or abnormal TD in 1 or more motor nerves	Evidence of unequivocal TD	Partial motor CB
(a) Partial conduction block <15% change in duration between proximal & distal sites &>20% drop in negative peak area of peak to peak amplitude between proximal & distal sites		pCMAP/dCMAP ratio <0.5 and dCMAP > or equal to 20% LLN
(b) Abnormal TD & possible CB >15% change in duration between proximal & distal sites & >20% drop in negative peak area or peak to peak amplitude between proximal & distal sites		
4. Absent F-waves or prolonged minimum F-wave latencies in 2 or more motor nerves	F-wave latency >120% of normal	F-wave latency >120% of ULN
(a) >120% ULN if amplitude >80% of LLN		
(b) >150% ULN if amplitude <80% of LLN		
Three of the above 4 should be present to make the diagnosis of GBS	One of the above 4 in 2 or more nerves during the first 2 weeks	At least 1 of the above 4 in at least 2 nerves, or at least 2 in 1 nerve if all others inexcitable & dCMAP 10% or more of LLN

CV=conduction velocity, LLN=lower limit of normal, ULN=upper limit of normal, DML= distal motor latency, CB= conduction block, TD= temporal dispersion, dCMAP=compound muscle action potential after distal stimulation, pCMAP= compound muscle action potential after proximal stimulation

Acute Motor Axonal Neuropathy

The electrophysiological hallmark of AMAN is the absence of or decrease in compound muscle action potentials to <80% of lower limit of normal. There should be no features of demyelination in motor conduction studies. Sensory nerve action potentials are also normal.[6,8,13]

Acute Motor Sensory Axonal Neuropathy

In AMSAN, both sensory nerve action potential and compound muscle action potential amplitudes are either reduced or absent. Motor terminal latencies and conduction velocities are still within normal limits.

Miller Fisher Syndrome

The most consistent finding is reduced or absent sensory nerve action potentials. Motor and sensory nerve conduction velocities are either normal or minimally slowed. The tibial H-reflex is usually absent. Denervation changes are absent in limb muscles on needle electromyography.[14] A moderate increase in F-wave latency and reduction in compound muscle action potential amplitude in motor conduction studies have been observed in some cases.[15] Reduction in central motor conduction time on transcranial magnetic stimulation which indicates corticospinal tract conduction abnormality has been reported.[16]

Sensory Guillain-Barré Syndrome

In the series of 8 patients reported by Oh *et al,* evidence of demyelination was seen in at least 2 nerves in all cases.[10] Seven patients demonstrated electrophysiological features of demyelination on motor conduction studies while 2 demonstrated such features on sensory conduction studies. Needle electromyography was normal in all subjects.[10]

In ASFSN, routine motor and sensory nerve conduction studies, which assess large diameter nerve fibre function, are essentially normal. Sympathetic skin response, which measures peripheral sympathetic conduction through small diameter unmyelinated fibres, has also been found to be normal. Quantitative sensory testing would be helpful in confirming the diagnosis of this entity.[11]

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