

AAEM PRACTICE TOPIC IN ELECTRODIAGNOSTIC MEDICINE

American Association of Electrodiagnostic Medicine

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ABSTRACT: At this time, there are no widely accepted criteria for the diagnosis of multifocal motor neuropathy. Furthermore, there is insufficient empirical data to define clinical and laboratory features that may reliably separate certain lower motor neuron syndromes with overlapping features as distinct. The AAEM therefore developed five criteria through a formal consensus process that are described in this document to act as a guide for diagnosing multifocal motor neuropathy with a high level of confidence (definite multifocal motor neuropathy) or with a moderate level of confidence (probable motor neuropathy). In brief, the diagnosis requires clinical weakness without objective sensory loss or upper motor neuron signs in the distribution of two or more named nerves that is due to conduction block in two or more motor nerves outside of common entrapment sites. Furthermore, normal results are required for sensory nerve conduction studies.

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CONSENSUS CRITERIA FOR THE DIAGNOSIS OF MULTIFOCAL MOTOR NEUROPATHY

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Multifocal motor neuropathy is a disease of lower motor neurons in adults that produces asymmetrical muscle weakness, often in association with fasciculations and cramping. Although the weakness caused by this uncommon disease is reversible with certain immunomodulating treatments, multifocal motor neuropathy may be mistaken for other, far more serious, disorders such as amyotrophic lateral sclerosis (ALS) that do not respond to immunotherapy. At this time, there are no widely accepted criteria for the diagnosis of multifocal motor neuropathy. Furthermore, there is

insufficient empirical data to define clinical and laboratory features that may reliably separate certain lower motor neuron syndromes with overlapping features as distinct. An expert panel of the American Association of Electrodiagnostic Medicine (AAEM) therefore developed this document to act as a guide for diagnosing the disease.

DESCRIPTION OF THE PROCESS

Physicians are often required to make diagnostic or therapeutic decisions for conditions in which empiric data and knowledge are incomplete or inconclusive. In such settings, the development of a consensus from an appropriate group of experts is often helpful in focusing research on critical questions and in providing interim guidance until the questions are answered empirically. Because the need for establishing consensus criteria is common, clinical health researchers have developed consensus methods over the past three decades.

A five-round modified Delphi process was used to develop these consensus criteria.⁴ The authors wrote an initial draft document, which was circulated for unsolicited comments from an expert panel. The expert panel was chosen from AAEM members who

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Table 1. Proposed criteria for partial conduction block.

Nerve segment (proximal/distal stimulation sites)	Minimal temporal dispersion (duration increased by 30% or less)				Moderate temporal dispersion (duration increased by 31 to 60%)	
	Definite partial conduction block		Probable partial conduction block		Probable partial conduction block	
	Amplitude reduction (%)	Area reduction (%)	Amplitude reduction (%)	Area reduction (%)	Amplitude reduction (%)	Area reduction (%)
Median						
Forearm (elbow/wrist)	>50	>40	40–49	30–39	>50	>40
Arm (axilla/elbow)	>50	>40	40–49	30–39	>50	>40
Proximal (EP/axilla)	Not accepted*	Not accepted*	>40	>30	>50	>40
Ulnar						
Forearm (below elbow/wrist)	>50	>40	40–49	30–39	>50	>40
Across elbow (above/below)	>50	>40	40–49	30–39	>50	>40
Arm (axilla/above elbow)	>50	>40	40–49	30–39	>50	>40
Proximal (EP/axilla)	Not accepted*	Not accepted*	>40	>30	>50	>40
Radial						
Forearm (elbow/distal forearm)	Not accepted*	Not accepted*	>50	>40	>50	>40
Arm (axilla/above elbow)	Not accepted*	Not accepted*	>50	>40	>50	>40
Proximal (EP/axilla)	Not accepted*	Not accepted*	>50	>40	>50	>40
Peroneal						
Leg (below fibular/ankle)	>60	>50	50–59	40–49	>60	>50
Across fibular head (above/below)	>50	>40	40–49	30–39	>50	>40
Thigh (SN/above fibular)	Not accepted*	Not accepted*	>50	>40	>60	>50
Tibial						
Leg (knee/ankle)	>60	>50	50–59	40–49	>60	>50
Thigh (SN/knee)	Not accepted*	Not accepted*	>50	>40	>60	>50

EP, Erb's point; SN, sciatic notch.

*Reproduced with the permission from reference 1, which can also be consulted for the reason that definite partial conduction block is not accepted for these segments.

had been authors of articles concerned with concepts relevant to multifocal motor neuropathy and who held divergent opinions at the start of the consensus development process. Based on the comments from the expert panel, and areas of apparent agreement and disagreement, the document was revised and recirculated until consensus was reached.

DIAGNOSING MULTIFOCAL MOTOR NEUROPATHY

Multifocal motor neuropathy is a diagnosis that is based on recognition of a characteristic pattern of clinical symptoms, clinical signs, and electrodiagnostic findings. The fundamental electrodiagnostic finding is partial conduction block of motor axons. Thus, this consensus statement relates closely to previously described criteria for the diagnosis of partial conduction block, reproduced in brief in Table 1.¹ The purpose of this consensus statement is the development of a definition for the circumstances by which multifocal motor neuropathy can be diagnosed with a high level of confidence (definite mul-

tifocal motor neuropathy) or with only a moderate level of confidence (probable multifocal motor neuropathy).

The criteria listed in Table 2 are intended to: (1) provide clinicians with diagnostic guidelines for the most typical patients, (2) propose diagnostic categories for research studies and clinical trials, and (3) stimulate further discussion about multifocal motor neuropathy. However, because these criteria are intentionally restrictive, clinicians might recommend treatment for some patients who do not satisfy these proposed criteria.

REVIEW OF THE LITERATURE ON MULTIFOCAL MOTOR NEUROPATHY

Multifocal motor neuropathy produces insidiously progressive weakness that is characteristically caused by persistent conduction block and is often associated with anti-GM1 ganglioside antibodies. Different authors first reported various aspects of the syndrome.^{3,8,12,13,18,19} Lewis and colleagues first de-

Table 2. Criteria for the diagnosis of multifocal motor neuropathy.

Criteria for definite multifocal motor neuropathy

1. Weakness without objective sensory loss in the distribution of two or more named nerves. During the early stages of symptomatic weakness, the historical or physical finding of diffuse, symmetric weakness excludes multifocal motor neuropathy.
2. Definite conduction block (see Table 1) is present in two or more nerves outside of common entrapment sites.*
3. Normal sensory nerve conduction velocity across the same segments with demonstrated motor conduction block.
4. Normal results for sensory nerve conduction studies on all tested nerves, with a minimum of three nerves tested. The absence of each of the following upper motor neuron signs: spastic tone, clonus, extensor plantar response, and pseudobulbar palsy.

Criteria for probable multifocal motor neuropathy

1. Weakness without objective sensory loss in the distribution of two or more named nerves. During the initial weeks of symptomatic weakness, the presence of diffuse, symmetric weakness excludes multifocal motor neuropathy.
2. The presence of either:
 - a. Probable conduction block in two or more motor nerve segments that are not common entrapment sites, or
 - b. Definite conduction block in one motor nerve segment and probable conduction block in a different motor nerve segment, neither of which segments are common entrapment sites.
3. Normal sensory nerve conduction velocity across the same segments with demonstrated motor conduction block, when this segment is technically feasible for study (that is, this is not required for segments proximal to axilla or popliteal fossa).
4. Normal results for sensory nerve conduction studies on all tested nerves, with a minimum of three nerves tested.
5. The absence of each of the following upper motor neuron signs: spastic tone, clonus, extensor plantar response, and pseudobulbar palsy.

*Median nerve at wrist; ulnar nerve at elbow or wrist; peroneal nerve at fibular head.

scribed a syndrome of chronic asymmetric weakness due to persistent motor conduction block in 5 of their 40 patients with chronic acquired demyelinating polyneuropathy.⁸ These five patients presented with pain and numbness in one or both hands. Parry and Clarke first described patients with chronic, asymmetric weakness due to persistent motor conduction block who did not have objective sensory abnormalities.^{12,13} Between the time that Parry and Clarke reported their finding on the two patients in an abstract and their finding on five patients in a full paper, Roth and colleagues reported two patients with asymmetric upper limb weakness without objective sensory involvement due to persistent motor conduction block.^{18,19}

Freddo and colleagues first recognized IgM antibody with activity directed against GM1 ganglioside

in a patient with lower motor neuron weakness and a monoclonal gammopathy in 1986.³ Parry and colleagues were the first to describe and pathologically confirm a patient with a syndrome resembling motor neuron disease associated with monoclonal IgM protein that appeared to be responsive to immunosuppression.¹⁴ Pestronk and colleagues reported two patients with a reversible syndrome of motor neuron disease in which both patients presented with asymmetric hand weakness without numbness due to persistent motor conduction block that was associated with high titers of IgM anti-GM1 ganglioside antibody without a monoclonal gammopathy.¹⁶ These two patients did not respond to treatment with prednisone and plasmapheresis, but did improve with cyclophosphamide. Pestronk and colleagues coined the term multifocal motor neuropathy in this article describing the association between multifocal motor neuropathy and anti-GM1 ganglioside antibodies.¹⁶

Typical clinical and laboratory features of multifocal motor neuropathy have emerged, starting with the 1990 publication of a report that included the first large series of patients with multifocal motor neuropathy.¹⁵ In this report, two-thirds of patients were men, and two-thirds were less than the age of 45. The report described that weakness usually begins in one hand and may remain restricted to that one hand for years or may gradually spread to all four limbs. Tendon reflexes may be brisk, especially early in the course of the disease; however, spasticity, clonus, extensor plantar responses, and pseudobulbar palsy do not occur. Cranial nerve signs are rare early in the course.⁵ Bulbar and respiratory involvement also is rare, but if this happens, it may eventually become life threatening.⁹ Fasciculations and cramping are common. Sensory function is normal by clinical and electrodiagnostic examination.

Because motor neuron disease and multifocal motor neuropathy have similar clinical features, patients are sometimes diagnosed with motor neuron disease rather than multifocal motor neuropathy. However, in contrast to motor neuron disease, all patients with multifocal motor neuropathy have partial conduction block of motor fibers, and many have high titers of anti-GM1 antibodies. Although weakness in multifocal motor neuropathy is characteristically caused by partial conduction block of motor fibers, degeneration of motor axons may contribute to weakness later in the course of multifocal motor neuropathy. This results in multifocal motor neuropathy having an even greater resemblance to motor neuron disease.

In contrast to motor neuron disease, patients with multifocal motor neuropathy usually respond to

treatment with intravenous immunoglobulin or cyclophosphamide.^{2,5} However, neither patients with multifocal motor neuropathy nor patients with motor neuron disease are expected to respond to prednisone or plasmapheresis.^{2,5}

Confusion with regard to the diagnosis of multifocal motor neuropathy is explained, in part, by its initial recognition from two different perspectives. Cases of weakness caused by persistent conduction block were first recognized among patients with chronic demyelinating polyneuropathy.⁸ Many later cases were identified among patients who were initially thought to have motor neuron disease.^{12,13}

The concept of multifocal motor neuropathy has also been confused, because different authors have applied a broad range of diagnostic criteria that vary in the (1) degree of sensory involvement, (2) requirement for partial conduction block, (3) electrophysiological criteria used for partial conduction block, and (4) requirement for anti-GM1 ganglioside antibodies. Some authors have applied broader, more inclusive criteria to diagnose multifocal motor neuropathy whereas other authors have applied narrower, more restrictive criteria. In reports by authors using the broad criteria, some cases have closely resembled multifocal motor neuropathy, except for the absence of partial conduction block.^{7,11} Other cases reported using the broad criteria seem typical for multifocal motor neuropathy, except for finding minor abnormalities on sensory nerve conduction studies.

The authors applying the narrower, more restrictive criteria have identified new syndromes that have lower motor neuron weakness and share features of, but are distinguished from, multifocal motor neuropathy. Three such proposed lower motor neuron syndromes are: (1) a syndrome that is associated with high titers of antiglycolipid antibodies and that has a similar absence of sensory and upper motor neuron features, but is not associated with conduction block^{15,17}; (2) Lewis-Sumner syndrome or multifocal acquired demyelinating sensory and motor neuropathy—a syndrome that has lower motor neuron weakness associated with sensory involvement due to multifocal conduction block^{10,20}; and (3) a syndrome that resembles multifocal motor neuropathy clinically, but has multifocal axon loss electrodiagnostically.⁶

Participants in this consensus process believe that multifocal motor neuropathy should be distinguished from chronic inflammatory demyelinating polyneuropathy but that sufficient empiric data and knowledge are not available at this time to determine if multifocal motor neuropathy is distinct from

the other lower motor neuron syndromes described above. The expert panel had the greatest difficulty in reaching consensus on the issue of excluding the diagnosis of multifocal motor neuropathy in cases with minor abnormality on sensory nerve conduction studies.

RECOMMENDATIONS FOR FUTURE RESEARCH

A strong consensus exists in the authors and expert panel that future research concerning the pathogenesis and treatment of multifocal motor neuropathy will be advanced through a narrow consensus definition, such as the one described in this article. Depending on the results of future research, other lower motor neuron syndromes may prove to be a variant of multifocal motor neuropathy, part of a spectrum of diseases closely related to multifocal motor neuropathy, or distinct clinical entities.

In conclusion, the diagnosis of multifocal motor neuropathy is a difficult one. Until further research clarifies the issue, the criteria for definitive and probable multifocal neuropathy listed in Table 2 are proposed to serve as a guide for diagnosing this disease.

DISCLAIMER

This report is provided as an educational service of the AAEM. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible methods of care of a particular clinical problem or all legitimate criteria for choosing to use a specific procedure; neither is it intended to exclude any reasonable alternative methodologies. The AAEM recognizes that specific patient care decisions are the prerogative of the patient and his/her physician and are based on all of the circumstances involved.

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