

Myopathies: Diagnostic Guidance and Correlations from EMG/NCS

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Introduction

Nerve conduction studies are generally unrevealing and provide no significant insights in patients with muscle disease. Electromyography (EMG) has always had some limitations in guiding diagnoses for muscle disease. With the increased availability and affordability of genetic testing, including panels, and recognition of MRI patterns that help to guide the diagnosis, EMG has taken even more of a backseat when it comes to muscle disease. However, the usefulness of EMG in myopathy is to focus the physician on the diagnosis of myopathy as a possibility. In the case of possible genetic disorders, it can guide the genetic testing done or correlate with the testing results. The electrophysiology and its correlation with the neuropathology is also confirming for a diagnosis. EMG cannot stand alone to diagnose muscle disease – it is still an extension of the clinical examination. It does not need to be done on every patient with muscle disease, but in some cases, the findings can completely re-focus the investigation and treatment possibilities. We will address some of the common findings in myopathy as well as the less common and how they can help with diagnosis.

General findings

Voluntary motor unit potentials (MUPs) in a patient with myopathy are classically described as small (<200mV amplitude), polyphasic and short duration. The underlying pathology that the physiology reflects is loss of muscle fibers and loss of synchronous firing of remaining muscle fibers. [1] With activation, there is early recruitment of MUPs – the normal ratio of number of motor units per firing rate is increased. More motor units are required to produce any given amount of force. With chronic myopathies, there may be loss of whole motor units, however, resulting in decreased recruitment as well. The size of the MUPs may help to avoid the interpretation of a neurogenic pattern but it can be difficult to distinguish. Chronic myopathies may have a mixed pattern due to reinnervation of healthy segments of muscle fibers via collateral sprouting. This may be reflected with similar pathology of mixed myopathic and neurogenic features. In addition, there is some normal variability in amplitude and recruitment in different muscles. This requires the experience of knowing what the normal findings in any given muscle should look like. For example, the iliopsoas muscle MUPs are smaller than those from the vastus lateralis muscle.

Normal MUPs can certainly be seen in myopathies and there is the importance of looking at muscles that are clinically weak. Even in these muscles, however, the abnormal voluntary MUPs are not the best clue to specific type of myopathy. It may redirect the planning of next steps.

Evaluation with EMG when there is a suspicion of myopathy requires looking at multiple muscles both distal and proximal, including muscles that are weak and not weak and to remember to include paraspinal muscles. This will give you the highest chance of 1) finding abnormalities 2) finding a distribution of abnormalities that helps to narrow down the diagnosis.

Spontaneous discharges

Electrodiagnostic findings at rest are much more helpful in a patient with muscle weakness than voluntary MUPs when attempting to distinguish between different causes. The only comment on insertional activity is that a decrease or absence of insertional activity in a particular muscle should point you away from biopsy of that muscle, as there is most likely significant fibrotic or fatty replacement of that muscle. Increased insertional activity is usually accompanied by other spontaneous discharges.

Fibrillation potentials are commonly associated with active denervation. When seen in a patient with suspected myopathy, it is a clue for active myositis. In muscle disease, fibrillation potentials indicate membrane irritability – segmental necrosis of muscle fibers resulting in separation of the healthy portion of the muscle fiber from the endplate. [2] The use of EMG to assess response to therapy with serial EMGs may be helpful in a patient

who has had improvement and then starts to deteriorate on high dose steroids. Early in disease, there are more fibrillation potentials and few if any myopathic units. These will both increase if untreated. Once treatment is begun, the fibrillation potentials are the first to respond, reducing in amount or resolving with the MUPs slowly decreasing but may not return to normal. [1] Key to looking for abnormal discharges in myopathies is looking at the paraspinal muscles – this is important in myositis when looking for fibrillation potentials but also in other disorders below. [3]

Myotonic discharges in a patient with myopathy raise other questions. Myotonic discharges are due to muscle membrane hyperexcitability resulting in repetitive firing after activation or stimulation (such as needle movement during EMG). In myopathies with clinical myotonia, finding electrical myotonia on EMG comes as no surprise. In those without clinical myotonia, it may be surprising and should turn the questioning towards possible diagnoses such as acid maltase deficiency, X-linked myopathy with excessive autophagy (XMEA) [4], thyroid-induced myopathy, and drug-induced myopathy (especially colchicine) [5]. [Table 1] Myotonic discharges have been described in myositis as well but are not as prominent.

Myotonic discharges are sustained firing of single muscle fibers in a rhythmic discharge that is waxing and waning with variable frequencies, up to 150 Hz. This is triggered by needle insertion or mild muscle contraction. Since the discharge originates from single muscle fibers, the appearance of the discharges is similar to fibrillation potentials or positive waves. The shape of the discharge, as with all needle EMG recordings, is based on the relationship spatially to the recording surface of the needle. The discharge will change shape and size as it moves towards and then away from the needle recording surface. The discharges will vary in amplitude in a range of 10 microvolts to 1 mV and a frequency variation of 50 – 100 Hz, often with an inverse relationship between size and frequency. [6] The sound is similar to the revving of a motorcycle engine, waxing and waning. If the firing is on the slow end of the spectrum, there is a risk that myotonic discharges may be mistaken for fibrillation potentials or positive waves, emphasizing the importance of taking time during the needle examination to try to characterize the spontaneous discharges. This can be a significant problem in myotonic dystrophy type 2 (DM2) patients, where the discharges can also be very short/brief and this mistaken interpretation occurs more easily.

The underlying mechanism for these prolonged discharges is based on chloride or sodium channel abnormalities or dysfunction. In some disorders with associated myotonic discharges, there is not a clear channel abnormality but the mechanism is presumed to be the same and the effect on the channel not fully understood. Decreased resting chloride conductance results in repetitive electrical discharges [7] The exact mechanism is still not completely clear; however, the predominant explanation is that chloride conductance stabilizes the membrane potential by shunting depolarizing current and dampening its effect. Abnormal chloride conductance increases resistance (R) which reduces the amount of current (I) needed to reach depolarization potential threshold (E) [Ohm's Law $E=IR$]. Resulting sodium channel opening initiates an action potential; delayed activation of potassium conductance hyperpolarizes the membrane and potassium accumulates in the T-tubule system. [6,8] Then, as potassium conductance returns to resting value, the cell is slightly depolarized. With abnormal chloride conductance, this can trigger another action potential, leading to repetitive action potentials. In the chloride channel disorders, there appears to be incomplete sodium channel inactivation and potassium ion accumulation in the T-tubules resulting in myotonia and weakness. In myotonic dystrophy type 1 (DM1), DM2 and myotonia congenita, there is an abnormality of the CLCN-1 chloride channel. The exact location of these channels in muscle fibers is still not completely clear. [8,9] In myotonia congenita, there is low chloride permeability that maintains the membrane instability, although this decreased permeability is not seen in DM1 or 2. [10]

At least in one study of DM1, there was a reported correlation between number of trinucleotide repeats (CTG) on *DMPK* gene and amount of myotonia. [11] This is not known to be the case in DM2 and clinical severity also does not appear to be correlated with number of CCTG repeats on *CNBP* gene in DM2. [12]

Abnormal sodium channels can also cause membrane instability and abnormal discharges, myotonia being just one of these discharges. A study by Drost et al identified that the morphology of myotonic discharges can distinguish between sodium and chloride non-dystrophic myotonia disorders. The first interdischarge interval was <30 ms in all of the sodium channelopathies and > 30 ms in all but one of the chloride channelopathies in a single muscle of 66 patients (32 chloride and 34 sodium channelopathies). [13]

In the hereditary sodium channel disorders, there is an associated mutation of the voltage-gated sodium channel alpha-subunit gene (SCN4A) and results in myotonia or paralysis. Sodium channel disorders with myotonic disorders include paramyotonia congenita, hyperkalemic periodic paralysis, and potassium-aggravated myotonia. The SCN4A mutations cause a gain of function defect, with more sodium current than normal passing through and causing an impairment of physiologic inactivation. [14] The myotonia is caused by a persistent slight depolarization with hyperexcitability. Paralysis may also occur with sustained depolarization block as seen in the paralytic part of hyperkalemic periodic paralysis or hypokalemic periodic paralysis type II.

Another interesting component of myotonia in these disorders is the “warming up” phenomenon. With voluntary action, myotonia may initially worsen but then with repeated activity, it will improve. The myotonia then recurs after a brief rest. Cold will worsen post-activation myotonia and percussion myotonia. [15] Cooling of muscles during EMG can bring out electrical myotonia. In addition, voluntary compound muscle action potentials may have decreased amplitudes and may become smaller after isometric exercise or repetitive stimulation. [16]

Specific disease clues:

Distinguishing types of inflammatory myopathies is best done by muscle biopsy. However, the distribution of abnormalities may give a clue with fibrillation potentials and abnormal MUPs in general more asymmetric and patchy in inclusion body myositis than in dermatomyositis or polymyositis. The presence of prominent fibrillation potentials in the setting of elevated CK and significant proximal muscle weakness is consistent with a necrotic myopathy as well.

Myotonic discharges are more prominent in myotonia congenita. Myotonic discharges in type 2 myotonic dystrophy are usually shorter bursts and less pronounced than in type 1. In either disorder, they may not be in all muscles. Fibrillation potentials and fasciculation potentials may also be seen and can sometimes be misleading or cause the myotonia to be overlooked. Cooling will bring out myotonic discharges in all three of these disorders as well as in paramyotonia congenita.

In patients with proximal muscle weakness, no clinical myotonia and elevated CK, the presence of myotonic discharges especially in the paraspinal muscles along with small MUPs in proximal muscles should raise the question of acid maltase deficiency. Other vacuolar myopathies should also be considered in the appropriate clinical setting.

Summary:

EMG is an extension of the clinical examination. In many myopathies, the clinical picture along with the family history precludes the need for EMG and may lead straight to genetic testing and/or muscle biopsy. The electrophysiology can be especially helpful when the possible diagnosis is less clear. The electrophysiology can also guide the need for genetic testing or muscle biopsy. The exact mechanisms for the electrophysiological findings are not always completely understood or explained by the pathophysiology but together, the electrophysiology and pathophysiology can lead to a diagnosis, potential treatment and prognosis for patients with myopathy.

**Table 1
Disorders with Myotonia**

With clinical myotonia	Inheritance
Myotonic dystrophy type 1	AD
Myotonic dystrophy type 2	AD
Myotonia congenita	AD and AR
Paramyotonia congenita	AD or de novo
Hyperkalemic periodic paralysis	AD
Without clinical myotonia	
Acid maltase deficiency	AR
XMEA	X-linked
Thyroid induced myopathy	-
Drug-induced myopathy (colchicine, glycyrrhizin)	-
Myositis	-

XMEA = X-linked myopathy with excessive autophagy

Modified from Kimura J. Electrodiagnosis in Diseases of Nerve and Muscle: Principles and Practice. 4th edition. 2013

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