Electrodiagnostic findings in myotonic dystrophy: A study on 12 patients

Ahmet Z. Burakgazi

Virginia Tech Carilion School of Medicine, Roanoke, VA, USA

Abstract

Myotonic dystrophy (DM) is a complex multisystem disease with specific clinical and electrodiagnostic findings. Myotonia can be seen in the distal and proximal muscle groups in upper and lower limbs. There is no established guideline to demonstrate the sensitivity of muscles in the diagnosis of myotonic dystrophy. The aims of this study are to describe common electrodiagnostic findings in patients with DM; and to assess the electrodiagnostic sensitivity of muscles in the diagnosis of DM. In this retrospective study, patients' age, sex, nerve conduction study findings including common upper and lower limbs nerve functions, and needle examination findings were collected and analyzed. A descriptive analysis (with percentage) was performed on the data obtained from the charts. NCS analysis showed more than half of patients had normal sensory and motor NCS findings. In 11 over 12 patients, sensory NCSs were within normal limits. Only one patient showed abnormal sensory responses. The most common abnormal NCS findings were decreased amplitude with normal latency and normal conduction velocity. The needle analysis showed distal muscles including first dorsal interosseous, abductor policies brevis, tibialis anterior, medial gastrocnemius and peroneal longus muscles are more sensitive in detecting myotonic discharges than proximal muscles including deltoid, triceps, vastus medialis and vastus lateralis. Our findings showed sensory nerve responses were usually within normal limits. The most common NCS abnormality showed decreased motor nerve amplitudes. The needle test showed myotonic discharges were more prominent in the distal muscles in upper and lower limbs.

Introduction

Myotonic dystrophy (DM) is a complex multisystem disease with specific clinical and electrodiagnostic findings.[1,2] DM is classified based on the age of onset and clinical characteristics. DM is a genetic disorder and occurs as a result of expansions of repeats of the certain trinucleotide on the responsible gene.[1,3] A specific electrodiagnostic finding, called myotonia, is seen in the needle part during electromyography (EMG) study. EMG myotonia has characteristic pattern and sound, a typical dive-bomber sound is heard instead of electrical silence while the recording needle inserting into muscle at rest.[1,3] Myotonia can be seen in the distal and proximal muscle groups in upper and lower limbs.[2] There is no established guideline to demonstrate the sensitivity of muscles in the diagnosis of myotonic dystrophy.

Myotonic dystrophy (DM) is an RNA-medicated multisystemic disorders and has two subtypes, type 1 (DM1) and type 2 (DM2). Different underlying genetic defects are described to cause the DM subtypes. DM1 is caused by a *DMPK* 3' untranslated region (3'UTR) CTG^{exp} and DM2 by an intronic $CCTG^{exp}$ in *CNBP*. Somatic expansion is related to pathological onset but there is no correlation between expansion size and disease severity. Several tissue system involvements are seen DM including skeletal muscle myotonia, weakness/wasting, conduction defect/block, cognitive decline, cataract, hearing impairment, insulin resistance, autoimmune disease, etc.[4]

RNA toxicity and its related consequences are the main underlying pathogenesis of DM.[5] Expanded trinucleotide repeat from the mutant DM alleles cause RNA toxicity. The most common expanded trinucleotide repeat is located in the untranslated region of the dystrophia myotonica protein kinase (*DMPK*) gene in DM type 1; and in first intron of the *ZNF9* (*CNBP*) gene in DM2. In the DM, the mutant RNA has important role in the pathogenesis of the disease that ending up with no translation in the cell. These repeat expansions may also cause toxic effects on the other genes besides DM1 and DM2 loci.[4,6] Given the accumulation of mutant RNAs in the nucleus alteration of RNA-binding protein activity, aberrant splicing and abnormal function of several genes, several abnormalities are seen in the body cells including skeletal muscle chloride channel, insulin receptor, and cardiac troponin. Expanded CUG or CCUG repeats may cause sequestration of Muscle blind-like (MBNL)1that causing alternate splicing of the B1N1 gene and skipping of muscle-specific exon 11 of BINI messenger RNA.[6] These RNA changes cause impairment of T-tubule and excitation-contraction coupling. Myotonia, the specific clinical and electrodiagnostic finding of the disease, occurs as a result of skeletal muscle chloride channel dysfunction that engendered by at the end of this process.[4]

In this study, we retrospectively analyzed electrodiagnostic features of patients with adult onset DM-type 1. The aims of this study are 1) to describe common electrodiagnostic findings in patients with myotonic dystrophy; and 2) to assess the electrodiagnostic sensitivity of muscles in the diagnosis of myotonic dystrophy.

Materials and Methods

This is a retrospective and descriptive study to aim to analyze clinical and electrodiagnostic features of patients with DM-type 1 whom previously seen in Carilion Clinic neurology clinic, Roanoke, VA. This study was approved by the local Institutional Review Board (IRB). Twelve charts of patients who were previously clinically diagnosed with DM type 1 and underwent electrodiagnostic tests in Carilion Clinic neurology outpatient clinic were retrospectively reviewed. The type of DM was made based on typical clinical findings and family history. Seven of these patients had genetic confirmation as well.

A routine electrodiagnostic (EDx) study, including nerve conduction studies (NCS) using standard laboratory techniques was performed by one board certified electromyographers. Limb's temperature was maintained at 32°C at the dorsum of the

Correspondence: Ahmet Z. Burakgazi, Neuroscience Section, Department of Medicine, Virginia Tech Carilion School of Medicine, 3 Riverside Circle, Roanoke, VA 24016, USA.
Tel.: +1.540-521-4592.
E-mail: drburakgazi@yahoo.com

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hand and foot. The NCS was performed by the same physician and an average of the bilateral nerve responses was used during data analysis. The NCS were performed under a uniform protocol using a Caldwell EMG machine that included bilateral medial and ulnar motor responses; bilateral radial, medial and radial sensory responses; bilateral sural and superficial sensory responses; and bilateral common peroneal and tibial motor responses in 11 subjects, only lower NCS was performed in one subject. Routine needle upper EMG studies included examination of deltoid, biceps, triceps, pronator teres, first dorsal interosseous (FDI), and abductor pollicis brevis (APB) muscles; and the needle lower EMG studies included vastus medialis (VM), vastus lateralis (VL), tibialis anterior (TA), peroneal longus (PL), and medial gastrocnemius (MGast) muscles. The upper and lower limbs needle tests were performed in 11 subjects and only the lower limb needle test was performed in one subject. Interpretation of the EMG was performed according to accepted guidelines in order to minimize inter-rater reliability. During interpretation, myotonic discharges were categorized from 1+ to 4+ scales based on amplitude, frequency, and prolongation.

Patients' age, sex, nerve conduction study findings including common upper and lower limbs nerve functions, and needle examination findings were collected and analyzed. A descriptive analysis was performed on the data obtained from the charts.

Results

Charts of twelve patients with diagnosed with adult onset myotonic dystrophy were reviewed. The mean of age was 53.3±15.2 years. Of the subjects, five were male; and seven were female. Twelve patients were clinically and electrodiagnostically were diagnosed with DM-type 1.

The NCS analysis showed normal sensory and motor NCS in seven subjects. Reduced amplitudes were detected in bilateral median motor, and right tibial motor nerves in the patient #1; in bilateral median motor, ulnar motor, tibial motor, and left peroneal motor nerves in the patient #5; in bilateral medical motor, bilateral tibial motor, bilateral ulnar motor, and bilateral peroneal motor nerves in the patient #6; and in right peroneal motor, bilateral tibial, and left ulnar nerves in the patient #7. The NCS of Patient #12 showed decreased amplitude in left peroneal motor nerve with decreased conduction velocity (CV); decreased amplitudes in bilateral tibial motor nerve with prolonged latency and decreased CV, and absent sensory responses in bilateral superficial peroneal and bilateral sural nerves.

The needle assessment of upper limbs showed deltoid and triceps muscles were negative for myotonic discharges in three subjects; and biceps and PT muscles were negative for myotonic discharges in one subject. Distal upper limbs muscles including FDI and APB were most active muscles for myotonic discharges and were presents in all 11 patients. The needle assessment of lower limbs in 12 patients showed VL and VM muscles were negative for myotonic discharges in five patients; and TA and PL muscles were negative for myotonic discharges in one patient. Distal lower limbs were more active for myotonic discharges in TA, PL, and MGast muscles. In two patients, MGast were silent, but in these patients MGast were atrophic and fibrotic. The needle findings are summarized in Table 1.

Discussion

EMG findings are a key element in the diagnosis of myotonic disorders.[3] Myotonic potentials are one of the most specific potentials seen on needle EMG test. Myotonia is often easier to detect on EMG test than on neurological examination.[3,7] In this study, we aimed to determine the common NCS findings and electrodiagnostic sensitivity of upper and lower limbs' muscles in the diagnosis of myotonic dystrophy. This is the first study to make in the literature to assess EDx findings in myotonic dystrophy.

NCS analysis showed more than half of patients had normal sensory and motor NCS findings. In 11 over 12 patients, sensory NCSs were within normal limits. Only one patient showed abnormal sensory responses. The most common abnormal NCS findings were decreased amplitude with normal latency and normal conduction velocity. The diminished amplitude of motor nerves may be related to muscle wasting or motor axonal damage. Sensory nerves functions are usually within normal limits in patients with myotonic dystrophy. There is no previous study to compare our findings. Our results showed peripheral neuropathy is uncommon in myotonic dystrophy.

Myotonic discharges are spontaneous discharges with a waxing and waning of amplitude and frequency.[1,3] The needle analysis showed distal muscles are more sensitive in detecting myotonic discharges than proximal muscles in both upper and

Table 1. This table demonstrates the summary of myotonic discharge findings of the patients in upper and lower limbs. Myotonic discharges are categorized from 1+ to 4+ scales based on amplitude, frequency, and prolongation.

			Deltoid		Triceps		Biceps		PT.		FDI		APB		VL		VM		TA		PL		MedGast	
	Age	Sex	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
Pt 1	37	M	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+
Pt 2	49	F	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+
Pt 3	31	F	Slt	Slt	Slt	Slt	1+	1+	2+	2+	3+	3+	3+	3+	Slt	Slt	Slt	Slt	3+	3+	3+	3+	3+	3+
Pt 4	41	M	2+	2+	2+	2+	2+	2+	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+	4+	4+	4+	4+	4+	4+
Pt 5	78	F	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+
Pt 6	65	M	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	Slt	Slt
Pt 7	68	F	1+	1+	1+	1+	1+	1+	2+	2+	2+	2+	2+	2+	1+	1+	1+	1+	2+	2+	1+	1+	Slt	Slt
Pt 8	36	M	3+	3+	3+	3+	3+	3+	3+	3+	4+	4+	4+	4+	Slt	Slt	Slt	Slt	2+	2+	2+	2+	3+	3+
Pt 9	64	F	Slt	Slt	Slt	Slt	1+	1+	1+	1+	2+	2+	2+	2+	Slt	Slt	Slt	Slt	1+	1+	1+	1+	2+	2+
Pt 10	59	F	Slt	Slt	Slt	Slt	Slt	Slt	Slt	Slt	2+	2+	2+	2+	Slt	Slt	Slt	Slt	1+	1+	1+	1+	2+	2+
Pt 11	46	F	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Slt	Slt	Slt	Slt	Slt	Slt	Slt	Slt	Slt	Slt	2+	2+
Pt 12	65	M	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+	2+

Pt: Patient; R: Right; L: Left; PT: Pronator Teres; FDI: first dorsal interosseous; APB: Abductor Pollicis Brevis; VL: Vastus Lateralis; VM: Vastus Medialis; TA: Tibialis Anterior; PL: Peroneus Longus; MedGast: medial gastrocnemius; Slt: Silent.

lower limbs. In fact, the needle test of proximal muscles can be within normal limits with silent spontaneous activities in patients with myotonic dystrophy. In two cases, the needle test was unusually silent in MedGast muscles but MedGast muscles were atrophic and fibrotic in those cases. These findings are expected in the clinical context of adult onset myotonic dystrophy since distal muscles are generally more affected than proximal muscles.

EDx test is most important diagnostic test in myotonic disorders.[2,3] Providers may diagnose myotonic disorder with EMG test for clinically subtle cases. DM 1 patients typically have distal motor weakness with associated clinical and electrical myotonia.[3,5,8] In our series, distal muscles showed more prominent myotonic discharges than proximal muscles. In some cases, medial gastrocnemius muscle was silent for myotonia in advances cases that may be related to muscle wasting and fibrosis. Myotonia may be detected in clinically asymptomatic proximal muscles.

Conclusions

This study shows distal muscles are more sensitive to demonstrate myotonia in DM1 patients. However proximal muscles should be assessed as well. Sensory nerve responses are usually normal in DM1 patients. Decreased motor amplitude is the most common NCS findings that may be related to muscle wasting or motor axonal damage. EMG test is key test in diagnosis of myotonic disorder, particularly in clinically subtle cases.

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