SHORT REPORT

ABSTRACT: Twenty-five Turkish patients with recessive myotonia congenita (RMC), 16 of whom had genetic confirmation, were studied. Nineteen had transient weakness. In the upper extremities, onset age of transient weakness was usually in the early teens. All untreated RMC patients had a compound muscle action potential decrement of ⩾25%, usually above 50%, with repetitive nerve stimulation at 10/s for 5 s. Patients with other nondystrophic diseases with myotonia, except 1 patient with dominant myotonia congenita, had no transient weakness and a CMAP decrement below 25%.
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TRANSIENT WEAKNESS AND COMPOUND MUSCLE ACTION POTENTIAL DECREMENT IN MYOTONIA CONGENITA

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Patients with the recessive form of myotonia congenita (RMC), i.e., Becker's recessive generalized myotonia,[2] often suffer from a peculiar transient weakness of their muscles that appears while the muscles are exercised after a period of rest.[1,3–5,8–18,20] Like the symptom of myotonia, the transient weakness virtually disappears with continued exercise. It was first described by Sabouraud et al.[17] in a patient with ''Thomsen's disease'' who would now be considered to have RMC.

Ricker et al.[11,12] showed that transient weakness and compound muscle action potential (CMAP) decrement were closely associated in RMC patients. Although the CMAP decrement was the greatest in patients with pronounced transient weakness,[1,6,11,12,14,18,19] a certain amount of decrease of the CMAP occurred in all forms of myotonia when the time of nerve stimulation was long enough.[1,3,7,12,18,19]

Attempts to define the distinguishing features of the CMAP decrement in single cases or a small series of patients included statements that it starts earlier,[1,19] is of greater magnitude,[1,12,14,18,19] occurs at lower stimulation frequencies,[1,6] and recovers later[18] in RMC. Rossi et al.[13] concluded that the lack of a decrement excludes RMC with certainty.

The aim of this study was to investigate transient weakness and CMAP decrement in a relatively large number of myotonia congenita patients. In 16 of the RMC patients the diagnosis was confirmed by determination of the mutations in one or both alleles of the muscle chloride channel gene.

PATIENTS AND METHODS

Twenty-five patients with RMC, 6 with dominant myotonia congenita (DMC), 1 with paramyotonia congenita (PC), and 1 with hyperkalemic periodic paralysis (HyperPP) were investigated. Clinical and electrophysiological studies were done at the University of Istanbul and molecular genetic studies at the University of Ulm.

Transient weakness was evaluated with manual muscle testing. Repetitive nerve stimulation of the ulnar nerve was performed at 10/s and 5/s for 5 s, recording from m. abductor digiti minimi. The amplitude of the smallest potential of the train was compared with that of the first one. Single stimulation

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Table 1. Clinical/genetic characteristics and electrophysiological results in various myotonic syndromes.

Family	Patient	Sex	Age (years)	Onset age (years)	TW	Decrement (10/s for 5 s)	Mutation*	Code†
Recessive myotonia congenita								
1	1	M	17	5	Y	71	N.F.	RGM 31
	2	M	14	5	N	69	N.F.	RGM 31
2	3	F	10	6	N	25	A415V/A415V	RGM 32
3	4	M	15	<1	Y	33	N.F.	RGM 33
4	5	M	17	5	Y	N.T.‡	T268M/G859D	RGM 35
5	6	M	35	8	Y	64	A415V/N.F.	RGM 36
6	7	M	26	4	Y	75	14 bp del/14 bp del	RGM 37
7	8	M	38	5	Y	92	A415V/A415V	RGM 38
	9	F	42	2	Y§	33	A415V/A415V	RGM 38
8	10	M	18	8	Y	87	A415V/N.F.	RGM 39
9	11	M	33	10	Y‖	77	G355R/G355R	RGM 41
10	12	M	20	12	N‖	56	R894X/R894X	RGM 42
11	13	M	16	2	Y	95	4 bp del/4 bp del	RGM 43
12	14	F	13	1	Y	93	N.F.	RGM 44
13	15	M	24	11	Y§‖	73	A415V/A415V	RGM 47
14	16	M	27	14	N‖	37	A415V/A415V	RGM 50
	17	M	30	5	Y	95	A415V/A415V	RGM 50
15	18	M	10	4	N	36	A415V/A415V	RGM 50
16	19	M	28	7	Y	73	1 bp del/N.F.	RGM 51
17	20	M	51	8	Y	82	4 bp del/4 bp del	RGM 52
18	21	M	15	10	N‖	18	N.F.	RGM 54
19	22	M	19	11	Y§	56	N.T.	RGM 91
20	23	M	14	4	Y	80	N.T.	RGM 98
21	24	M	17	8	Y	95	N.T.	RGM 110
22	25	M	15	12	Y	75	N.T.	RGM 111
Dominant myotonia congenita								
23	26	M	33	1	N	20	N.F.	MC 17
24	27	M	11	1	N	10	G200R	RGM 34
	28	M	27	17	N	0	G200R	RGM 34
25	29	M	29	12	N	9	N.F.	RGM 40
26	30	M	39	18	N	10	N.F.	MC 50
27	31	M	18	3	Y	89	N.T.	MC 56
Paramyotonia congenita								
28	32	F	30	2	N	0	F1473S (SCN4A)	PC 28
Hyperkalemic periodic paralysis								
29	33	F	14	2	N	0	T704M (SCN4A)	HyperPP 28

Families 14 and 15 are related.
TW, transient weakness; Y, yes (present); N, no (absent); N.F., all exons screened and no mutations found; N.T., not tested or not investigated; bp, base pair; del, deletion.
**Mutations are in the gene coding for the muscle chloride channel (CLCN1) unless specified.*
†Code given at Ulm University.
‡82% at 5/s for 5 s.
§Very mild transient weakness.
‖On mexiletine.

after 10 s of exercise[18] was also done. Measurements were made from baseline to negative peak. Care was taken to allow at least 5 min between trains of stimuli.

RESULTS

Transient Weakness. Nineteen of the 25 patients with RMC, 1 with DMC, and none with PC/HyperPP had transient weakness by clinical examination. The distinguishing feature of transient weakness was that the first one or two muscle contractions after a period of rest were normal or slightly weak. Muscle strength suddenly decreased thereafter, remained decreased for several more contractions, and was usually restored to baseline within about 20 contractions. It was present in both upper and lower extremities. In 9 patients, some weakness persisted, especially in hand muscles.

Transient weakness was perceived by the patients as a sudden lapse of power during sustained activity after rest. The patients sometimes would have to drop a heavy weight after an initial lift. They could lift it again after working with the muscle for a while. This experience was clearly different from the myo-

tonic stiffness which they could also describe very well. In contrast, they could not define a symptom in the lower extremities which they could easily distinguish from myotonia, although transient weakness was also elicited in the lower extremities during the exam.

Patients with RMC became aware of transient weakness during their early teens. Three youths whose myotonia was not yet evident in the upper extremities had no transient weakness. One of them had no weakness during his first examination at age 14, but developed marked transient weakness when reexamined at 17.

One older mildly affected female patient with RMC had minimal transient weakness. Patients on antimyotonia drugs, except 1 who did not benefit from it, had no or little transient weakness.

CMAP Decrement. At 10/s, all RMC patients except 1 treated patient had a decrement ≥25% (Table 1). The mean decrement was 66.3%. In 8 patients, the mean decrement was reduced from 77% to 17.5% when the stimulation was performed after 1 min of exercise. The mean decrement was 21.6% (range: 0–82%) at 5/s and 29% (range: 0–86%) with single stimulation after 10 s of exercise. The decrement was larger with 10/s in each patient when compared to 5/s and in all but 1 when compared to single stimulation.

All patients with other nondystrophic myotonia except 1 patient with DMC had a decrement <25% at 10/s; the mean decrement was 7% (range: 0–20%), excluding the DMC patient with transient weakness who had a decrement of 89%. The mean decrement was 3.4% (range: 0–9%) at 5/s and 7.3% (range: 0–36%) with single stimulation.

DISCUSSION

In RMC, myotonia usually increases with age, both in severity and in distribution, initially being confined to the legs, then involving the arms, and then the cranial muscles in an ascending fashion.[2] Transient weakness also seemed to be age-related, particularly in the upper extremities. It was a relatively late symptom of the disease, making its appearance in the early teens, after the onset of myotonia in the hands. Thus, transient weakness did not seem to be evident in a particular muscle at the time when myotonia was mild or absent.

In addition to young patients, RMC patients with mild myotonic symptoms, including those benefiting from antimyotonia drugs, had no transient weakness or only a mild form of it. Patients with other nondystrophic diseases with myotonia, also suffering from less severe myotonia, had no transient weakness. The only exception was a patient with DMC who had transient weakness.

A correlation between myotonic stiffness and weakness is not surprising on the basis of the currently accepted pathomechanisms of the two symptoms. The reduced chloride conductance is thought to cause a transient membrane depolarization of the muscle fibers, which results in repetitive activity (the basis of stiffness) when mild and hypoexcitability (the basis of weakness) when severe.[12,14–16,18]

The most sensitive method in bringing out the decrement was 10/s for 5 s. All untreated and most of the treated RMC patients, with or without transient weakness, had a decrement ≥25% and usually >50%. The magnitude of decrement usually correlated with the amount of transient weakness. Other nondystrophic myotonia patients had no decrement or a decrement of <25% except the DMC patient with transient weakness who had a large decrement.

Based on our findings, the presence of a large decrement obtained at 10/s for 5 s suggests RMC, although an occasional DMC patient may have a large decrement. With a small decrement, nondystrophic myotonia other than RMC is more likely, unless the patient with RMC has very mild symptoms.

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