SHORT REPORT

ABSTRACT: We investigated electrophysiologically the unaffected parents of patients with recessive myotonia congenita. We studied 18 families, in nine of which the diagnosis was confirmed by molecular genetics. Brief myotonic discharges were present in at least one parent in 67% of the families. Fathers were more likely than mothers to show these discharges. The difficulty in distinguishing very mildly affected parents with dominant myotonia congenita from the heterozygous carriers of recessive myotonia congenita is stressed.

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ELECTRICAL MYOTONIA IN HETEROZYGOUS CARRIERS OF RECESSIVE MYOTONIA CONGENITA

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The recessive type of myotonia congenita (RMC), described by Becker,[2] is more common than the dominant type (Thomsen's disease).[2] In RMC, myotonia has a later onset (4–12 years) and usually commences in the legs, spreading after a variable interval (sometimes of years) to the arms and then to the face: it is more severe and is usually associated with transient weakness.[2] Not every RMC patient conforms to this pattern and it is sometimes difficult to decide clinically whether a patient has the recessive or the dominant form. The single factor by which RMC can be clinically differentiated with relative certainty from dominant myotonia congenita is the absence of clinical myotonia in the parents. The presence of myotonic discharges on needle electromyography (electrical myotonia) of the parents, however, is compatible with the diagnosis of RMC.[3] Although such an electromyographic finding in the parents is generally considered to be a manifestation of heterozygosity,[3] the possibility of its pointing to the presence of dominant type of inheritance has not been completely excluded.[9]

The aim of this study was to search for electrical myotonia in the parents of patients with RMC. In nine families, the diagnosis was confirmed by determination of mutations in one or two alleles of the muscle chloride channel gene in the patient.

MATERIAL AND METHODS

The electrophysiological work was done at the Department of Neurology, University of Istanbul and the molecular biology at the Department of Physiology, University of Ulm. Consent was obtained from the Review Committees of both institutions. Eighteen families of 21 patients were studied; sibling pairs were present in three families. Seventeen patients (81%) were male. Consanquinity was present in 11 families (61%). None of the parents had myotonia by history or clinical examination.

Three muscles, abductor pollicis brevis, flexor pollicis longus, and tibialis anterior, were tested in each of the parents. In each muscle, a minimum of eight sectors were examined at different depths by needle electromyography.

RESULTS

Myotonic Discharges. Myotonic discharges were present in at least one parent in 12 of the 18 families

Abbreviations: EMG, electromyography; RMC, recessive myotonia congenita

Key words: electrical myotonia; heterozygous carrier; recessiv myotonia congenita; recessive generalized myotonia

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(67%). They were present in 4 of the 17 mothers (24%) and 10 of the 14 fathers (71%) whom we examined. In two families, both parents had myotonic discharges (Table 1). Myotonic discharges were low amplitude and brief. They usually lasted for less than 1000 ms, but rarely persisted for several seconds. They were not very abundant except in an occasional parent. In 10 parents, only one muscle showed myotonic discharges; this was usually the abductor pollicis brevis muscle (Table 1).

There was no correlation between the presence, absence, or amount of myotonia and the genetic results. Parents with the same mutation (A415V/A415V) had different degrees of myotonic discharges or none.

Other Pathological Spontaneous Activity. Very brief complex repetitive discharges, short runs of positive waves, and increased insertional activity were also seen. Of note were prolonged trains of rhythmic, low-frequency (<60 Hz), biphasic activity (positive waves), lasting several seconds, sometimes changing in frequency and amplitude toward the end of the train without loss of rhythmicity. A parent with myotonic discharges usually also had all or most of the other types of activity, though to different degrees.

DISCUSSION

A search of the literature reveals that myotonic discharges have been reported in only three sets of parents of patients with RMC,[1–3,9] whereas seven sets of parents had normal needle electromyography (EMG) except—in some instances—for increased insertional activity.[1–3,4,7–9] In our study, needle EMG was abnormal in at least one parent in 67% of families. As described previously,[1–3] the myotonic discharges were of low amplitude and very short dura-

Table 1. Electrophysiological and genetic results in the parents of patients with RMC.

		Electrical myotonia*		Genetic results in the patient	
Family	Consanguinity	Mother	Father	Mutation†	Code‡
1	Yes	+ (APB)	+ (FPL)	NF/NF	RGM 31
2	Yes	–	+ (APB, FPL, TA)	A415V/A415V	RGM 32
3	Yes	–	–	NF/NF	RGM 33
4	No	+ (APB)	+ (APB)	T268M/G859D	RGM 35
5	Yes	–	+ (APB)	14 bp del/14 bp del	RGM 37
6	No	–	NT§	A415V/NF	RGM 39
7	Yes	–	+ (APB, FPL)	4 bp del/4 bp del	RGM 43
8	Yes	–	–	NF/NF	RGM 44
9	No	–	NT§	A415V/A415V	RGM 47
10	No	–	–	A415V/A415V	RGM 50
11	Yes	–	+ (APB)	A415V/A415V	RGM 50
12	No	+ (TA)	NT§	4 bp del/4 bp del	RGM 52
13	Yes	–	+ (FPL)	NF/NF	RGM 54
14	Yes	+ (APB)	NT§	NF/NF	RGM 82
15	No	–	–	NF/NF	RGM 83
16	Yes	NT	+ (APB, FPL, TA)	NF/NF	RGM 91
17	No	–	+ (APB, FPL, TA)	NF/NF	RGM 92
18	Yes	–	+ (APB)	NF/NF	RGM 94

Families 10 and 11 are related. +, present; –, absent, APB, abductor pollicis brevis; FPL, flexor pollicis longus; TA, tibialis anterior; NT, not tested; NF, not found (all exons screened and no mutations found); bp, base pair; del, deletion.
**In parentheses are the muscles with myotonic discharges.*
†Point mutations or deletions in the gene coding for the muscle chloride channels (CLCN1).
‡Code given at Ulm University.
§Dead.

tion. They were usually not very abundant, and not all muscles showed the abnormal activity to the same extent. Thus, it is possible that some of the so-called normal parents would have had abnormalities if more muscles had been tested, and our percentage of positive results may therefore be an underestimate. It is, however, important not to overinterpret minimal EMG abnormalities.[8,10]

It has previously been speculated that myotonic discharges in the parent are a sign of heterozygosity,[3] but this could not be corroborated with genetic studies at the time. We were able to identify the genetic defect in some of our patients, and some patents who were definite heterozygous carriers of the recessive trait (fathers in families 2, 4, 5, 7, and 11; mothers in families 4 and 12) had myotonic discharges, thus confirming this hypothesis. However, not all parents who were heterozygote carriers genetically (father in family 10; mothers in families 2, 5, 7, 9, 10, and 11) had myotonic discharges.

An interesting result of our study was that myotonic discharges were more likely to be found in fathers than mother.[6] RMC is known to occur more frequently in males.[2] Thus, a male preponderance of electrical myotonia in the parents accords with the male preponderance of symptomatic RMC patients.

Becker[2] commented that mothers with minimal but unquestionable symptoms of myotonia are more likely to be considered as affected, since females are generally less severely affected than males. We have studied a family, not included here, in which the mother of the affected child, initially considered to have RMC, had abundant myotonic discharges. She later admitted to having a few episodes of myotonia during pregnancy. Several other members of the family had also experienced mild myotonic symptoms. Genetic studies in this family were consistent with dominant type of inheritance.[6] Indeed, patients with dominant myotonia congenita can sometimes have very mild symptoms[5] that they tend to ignore.

Our study shows that the presence of electrical myotonia in the parents of a patient with myotonia congenita is perfectly compatible with recessive inheritance, although electromyographic examination cannot pick up all genetically confirmed heterozygote carriers. Electromyography alone can also not distinguish between recessive and dominant inheritance. The presence of abundant myotonic discharges, however, especially in the mother, should prompt the clinician to search more carefully for historical clues pointing to dominant inheritance. Thus, differentiation between these two myotonic entities is still dependent on the clinical history combined with genetic studies in selected cases.

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