ORIGINAL CONTRIBUTION

Proximal Myotonic Myopathy

Clinical Features of a Multisystem Disorder Similar to Myotonic Dystrophy

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Background: Previous investigations in three families have shown that proximal myotonic myopathy (PROMM) is not linked to the gene loci for myotonic dystrophy (DM) or to the loci of the genes of the muscle sodium and chloride channels associated with other myotonic disorders. It is important to extend our clinical knowledge of this interesting new disorder by studying other families.

Patients: Thirty-five patients in 14 new families; 27 patients were examined.

Methods: Clinical examination, electromyography, muscle biopsy, DNA analysis.

Results: The following findings were noted: proximal without distal weakness of the legs (n=21); myotonia on electromyograms (n=23); intermittent clinical myotonia (n=17); cataracts (n=24) and a number of the cataracts were identical to the type in DM (n=11); and peculiar muscle pain (n=14). A few patients had cardiac arrhythmias, and others had elevations in the concentrations of serum γ-glutamyltransferase. None of the patients had significant muscle atrophy. Muscle biopsy specimens showed mild myopathic changes. All patients had normal trinucleotide (cytosine, thymine, and guanine) repeat size of the DM gene in leukocyte DNA. Muscle DNA probes from three patients showed findings identical to those of their leukocyte DNA probes.

Conclusions: Proximal myotonic myopathy is a new genetic disorder similar to, but distinct from, DM. Patients suspected of having DM but with negative DNA studies may have PROMM. The gene defect for PROMM awaits discovery. Because of the similarities between PROMM and DM, this discovery will not only shed light on the pathomechanism of PROMM, but it may also increase our understanding of DM.

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A RECENT article by Thornton et al[1] has described three patients from two families with an autosomal dominant disorder, which they thought to be atypical myotonic dystrophy (DM). These patients had features of DM such as myotonia, cataracts, baldness, cardiac conduction disturbances, and testicular atrophy. They also had features atypical of DM, like proximal muscle weakness without distal weakness and muscular hypertrophy. The DNA analysis of the gene responsible for DM showed no abnormal trinucleotide (cytosine, thymine, and guanine [CTG]) repeat enlargement. In a subsequent study, on three further families with 15 patients, Ricker et al[2] excluded, by linkage analysis, the gene locus for DM on chromosome 19,[3-5] the gene locus responsible for paramyotonia (chromosome 17, skeletal muscle sodium channel),[6-9] and the gene locus for myotonia congenita (chromosome 7, skeletal muscle chloride channel).[10,11] They concluded that there exists a new genetic disorder, which they named *proximal myotonic myopathy* (PROMM). We now describe the evaluation of 27 affected individuals from 14 new families. Proximal myotonic myopathy appears to be a multisystem disease that is similar to, but distinct from, DM.

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REPORT OF CASES

Patient 3-1, the mother of two daughters, began to have intermittent myotonic stiffness in her thigh muscles when she was 38 years old. At 43 years of age, she developed grip myotonia that occurred oc-

See Patients and Methods on next page

PATIENTS AND METHODS

PATIENTS

Fourteen families were studied (**Table 1**). Autosomal dominant inheritance was apparent in 11 families. In three families, the affected individuals appeared to represent sporadic cases. However, because of death or the unavailability of family members, dominant inheritance could not be excluded. Thirty-five affected individuals were identified, and 27 had a neurologic evaluation, including an electromyographic (EMG) examination. Nine patients gave informed consent for muscle biopsy for histologic analysis and, in three cases, for muscle DNA analysis. Electrophysiologic in vitro studies of muscle fibers have already been performed in one case (case 7-1) and the results have been published.[12]

DNA STUDIES

The genomic DNA samples obtained from the patients were prepared from peripheral blood samples and, in three cases, also from muscle tissue using conventional methods.[13] To test for abnormal CTG expansion at the DM gene locus, genomic DNA was digested with the restriction enzymes *Eco*RI and *Bgl*I, subjected to electrophoresis, and transferred to nylon membranes. The Southern blot specimens were hybridized with the pM10M6 probe.[3,14] To determine the accurate size of the CTG repeat in the alleles from each individual, we performed a fluorescent polymerase chain reaction (PCR) with DM101 and DM102 as primers.[3] The primer DM101 was labeled with FAM. The PCR products were subsequently analyzed on an automatic DNA sequencer (ABI 373A, Applied Biosystems Inc, Foster, Calif), with Genescan software (Applied Biosystems Inc); Genescan 2500 (ROX) was used as the internal standard.

casionally and sometimes involved only one hand. At times she would drop objects. Infrequently, the myotonic stiffness in her legs would develop to a point that caused her to fall, but on other days she had no myotonia. Since the age of 44 years, the patient had muscle pain, primarily in the thighs, calves, and upper arms. This pain was not consistent. She had proximal leg weakness and was unable to arise from a squat without assistance. Shoulder abduction, elbow extension, and forward head flexion showed mild weakness. She had mild grip myotonia, involving especially the index finger and the thumb, and mild myotonia after forceful eye closure. There was no muscle atrophy, sensory deficit, or cerebellar dysfunction. Tendon reflexes were normal. Electromyographic study of several muscles showed myotonic discharges. Motor and sensory nerve conductions were normal. A computed tomographic scan of the thigh muscles revealed no muscular atrophy or other abnormality. Slit-lamp examination showed cataracts with multiple-colored, subcapsular opacities. An electrocardiogram was normal. Results of blood studies showed a normal creatine kinase concentration. The γ-glutamyltransferase level was elevated (Table 1), while levels of alanine aminotransaminase and aspartate aminotransaminase were normal. Thyroid gland function was normal.

The patient's half-brother (patient 3-3) developed intermittent myotonic stiffness in his thigh muscles at 35 years of age. Later on, he was affected in a similar manner as his half-sister. Her mother (patient 3-2) began to have difficulty arising from a squat at 50 years of age, and at 60 years of age she had to pull herself upstairs using the handrail. On flat ground, she was able to walk without problems. At 58 years of age, she had cataracts removed from both eyes.

RESULTS

CLINICAL OVERVIEW

A summary of clinical findings is given in **Table 2**. Initial symptoms occurred mostly between 20 and 60 years of age. A number of patients had myotonic stiffness in the thigh muscles and in their grip. Some patients complained of an annoying pain in their muscles, especially in the thighs. Some patients gradually developed proximal weakness in their legs. For other patients, the identification of cataracts was the first manifestation of this disorder.

Clinical Myotonia

Seventeen patients from 12 families had a history of clinical myotonia, although at the time of examination some of the individuals did not have clinical signs of myotonia. All of the individuals had myotonic discharges on EMG. Eight patients first noticed the presence of myotonia in their hands, sometimes in just one hand. Nine patients first noticed myotonic stiffness in their legs, primarily in the thigh muscles; one patient (patient 11-1) first noticed it in his toes. Within months to some years, all of the patients developed more widespread myotonia. Some patients noticed myotonia in the muscles of mastication or in the neck muscles. A few patients had brief generalized myotonia after performing a quick, strenuous jump. The myotonia was not present constantly. For days or even weeks, they had no myotonia. Sometimes a vigorous muscle contraction could bring about myotonia. There was a "warm-up" phenomenon with repeated muscle contractions. The quality of the myotonia was somewhat unique, in that patients with grip myotonia showed a stepwise, jerky relaxation of the fingers, especially of the index finger and thumb. Twelve patients had no history of clinical myotonia. Eight of these patients had myotonic discharges on EMG, although the discharges were sometimes scarce and difficult to detect. No electrical myotonia was found in four patients.

Electromyography

The EMG study revealed a pattern of spontaneous activity that is typically termed *myotonic discharges*. In addition, in several patients there were runs of complex re-

Table 1. Proximal Myotonic Myopathy: Summary of Clinical and Laboratory Findings*

Family-Patient No./ Sex/Age, y/Relation	Age at Onset of Symptoms, y	History of Clinical Myotonia	EMG Myotonia	Muscle Pain	Onset of Weakness Decade	Muscle Biopsy	CK, IU/L	γGT, IU/L	Cataract		
									Present	Age at Detection, y	Surgery
1-1/F/46/Proband	27	+	+	+	3	Biceps	109	19	+	45	...
1-2†/M/76/Father	65	...	ND	...	–	...	...	...	+	65	+
1-3/M/52/Brother	43	–	+	...	5	...	91	38	...	...	...
2-1/F/54/Proband	24	–	+	–	3	...	60	85	+	27	+
2-2/M/85/Father	...	–	–	–	7	...	63	8	–	...	...
3-1/F/44/Proband	38	+	+	+	5	...	61	42	+‡	44	...
3-2†/F/73/Mother	50	...	ND	...	6	...	...	...	+	58	+
3-3/M/57/Half-brother	35	+	+	+	5	...	205	29	+‡	55	...
4-1/F/66/Proband	35	–	+	+	4	Quadriceps	85	56	+	40	+
4-2/M/40/Son	38	+	+	–	–	...	107	...	...	...	...
4-3/M/51/Brother	...	–	+	...	–	...	121	78	...	...	...
4-4/F/51/Half-sister	...	–	+	...	–	...	85	...	+	45	+
5-1/F/40/Proband	37	+	+	+	4	Quadriceps	70	63	–	...	...
5-2/M/64/Father	...	+	ND	+	5	...	...	...	...	...	...
6-1/F/50/Proband	41	+	+	+	5	Biceps	320	183	+‡	46	...
6-2/M/29/Son	...	–	+	–	–	...	68	33	–	...	...
6-3†/M/55/Brother	38	+	+	+	4	...	90	...	+‡	54	...
6-4†/F/54/Mother	...	...	ND	...	–	...	...	...	+	48	+
7-1/M/76/Proband	15	+	+	–	3	Quadriceps	110	10	+	26	+
8-1/F/45/Proband	17	+	+	+	4	Biceps	60	...	–	...	...
8-2†/M/70/Father	...	...	ND	...	6	...	...	...	+	50	+
9-1/M/43/Proband	36	+	+	+	5	Biceps	260	...	+‡	41	...
10-1/M/56/Proband	37	+	+	+	5	Biceps	190	28	+‡	48	+
10-2/F/91/Mother	...	–	–	–	8	...	...	...	+	80	+
10-3/F/72/Sister	...	–	–	–	–	...	...	...	+	69	+
10-4/F/26/Daughter	23	+	+	–	–	...	89	30	–	...	...
11-1/M/27/Proband	22	+	+	+	–	...	362	18	–	...	...
11-2/M/31/Brother	25	–	+	+	–	...	629	25	–	...	...
11-3†/F/79/Grandmother	...	...	ND	...	6	...	...	...	+	65	+
12-1/M/40/Proband	23	+	+	+	4	Triceps	1120	58	+‡	26	...
13-1/M/44/Proband	44	–	–	–	–	...	52	...	+‡	37	...
13-2/M/18/Son	18	–	+	–	–	...	56	...	+‡	18	...
14-1/M/35/Proband	23	+	+	+	–	...	2800	128	+‡	33	...
14-2/F/54/Mother	25	+	+	+	5	...	114	34	+‡	52	...
14-3†/F/60/Grandmother	...	...	ND	...	5	...	...	...	+	48	...

*EMG indicates electromyography; CK, creatine kinase (normal values do not exceed 80 IU/L); γGT, γ-glutamyltransferase (normal values do not exceed 18 IU/L); plus sign, finding present; ND, not done; and minus sign, finding not present.

†Deceased.

‡Cataracts were indistinguishable from those typically seen in myotonic dystrophy (posterior capsular, iridescent multicolored opacities).

petitive discharges, and in a few patients brief runs (up to 1 second) of very-high-frequency (180 to 240 Hz) single-spike discharges were seen. Quantitative analysis of motor unit potentials was not attempted. Evaluation of the EMG pattern suggested mild myopathic changes in the thigh muscles that were studied.

Weakness

Twenty-one patients had weakness. Most of them recalled that the weakness first developed gradually during the fourth or fifth decades (Table 1). All 21 patients developed proximal leg weakness without significant atrophy. In the majority of patients, the weakness was very slowly progressive. In one patient (patient 6-1), there was a more rapid development of weakness over a 3-year period. Thirteen of the 21 patients could not arise from a squat unless they used their hands or other maneuvers. Eight patients could arise without assistance, but this required considerable effort. None of the patients had difficulty walking; 10 patients had, in addition to proximal leg weakness, weakness of the muscles in the anterior part of the neck; nine patients had weakness of arm abduction; and seven patients had weakness of elbow extensors, being unable to perform a push-up. Three patients could not sit up from the supine position without turning to their side or using assistance. None of the patients had weakness of the hands, feet, and facial muscles, and none had distinct muscular atrophy, although some reported that the muscle volume of their thighs had decreased. There was hypertrophy of the calf muscles in four patients, and in two of them it was clearly asymmetric.

Four patients had peculiar variations in their strength. Sometimes they would have more weakness lasting hours or days, or, in one patient (patient 1-3), a few weeks. During periods of increased weakness, repeated exercise would lead to an improvement in strength for a limited period of time, typically lasting half an hour. Four other patients complained of an increased, generalized

muscular fatigue, eg, when holding their arms above their head or carrying items for several minutes. Because of this fatigue, two patients (patient 1-1 and patient 6-1), underwent repetitive stimulation testing and one patient (patient 6-1) underwent measurement of the acetylcholine receptor antibody titer with normal results.

Muscle Pain

Fourteen patients complained of muscle pain. In the majority of patients, this pain occurred later in the illness. Only in patients 10-1 and 10-2 was pain the initial symptom. The pain occurred mainly in the thigh muscles and in the muscles of the upper arms and shoulders. It might be present on some days and then disappear for several days or even weeks. The presence of pain was not related to the myotonic stiffness. It was most apparent at rest. Patients described the quality of the pain as burning, tearing, or jabbing. The intensity varied from "unpleasant" to "hard to bear." Five of these 14 patients (patients 8-1, 11-2, 12-1, 14-1, and 14-2) had an increased sensitivity to being hit in their muscles. Following a blow to the muscle, they would have local pain that persisted for 20 to 30 minutes. Three patients (patients 9-1, 10-1, and 11-1) had some episodes of peculiar chest pain that could not be explained by cardiac causes.

Cataract

Twenty-four patients had cataracts, and in 16 patients the cataracts were identified before the age of 50 years (Table 1). Eleven of these patients had cataracts that had the typical features of the cataracts seen in DM, with posterior capsular, iridescent, multicolored opacities. The cataract had nonspecific, white-spotted capsular densities in two patients (patients 1-1 and 10-3). No description of the cataract was available in 11 patients. Patients had either died or the cataract had been removed previously.

Cardiac Involvement

Two patients from two families had the early onset of cardiac arrhythmias. One patient (patient 1-1) immediately after the birth of her second child, at 27 years of age, had a cardiac arrest. At 41 years of age, she developed severe cardiac arrhythmia for several weeks and a right bundle branch block was noted on her electrocardiogram. The other patient (patient 13-1) required treatment with a subcutaneous permanent pacemaker for heart block at 38 years of age.

Anticipation

There were 11 parent-child pairs of affected individuals in 11 families. In seven of these pairs, the child was more severely affected than the parent, having an earlier onset with more severe weakness. In the four remaining pairs, the patterns of clinical manifestations were similar for the parent and the child. There were no differences between male and female patients in the age at onset of disease or in the severity of disease.

Table 2. CTG Repeat Size of the DM Gene in PROMM*

Family-Patient No.†	No. of CTG Repeats for Both Alleles‡
1-1	5/12
2-1	12/21
3-1	5/5
4-3	5/10
5-1	10/11
6-1	12/13
7-1	5/17
8-1	5/12
9-1	5/5
10-4	5/20
11-1	10/13
12-1	5/13
13-1	5/24
14-2	12/18

*CTG indicates cytosine, thymine, and guanine, which are the bases associated with each of the three nucleotides; DM, myotonic dystrophy; and PROMM, proximal myotonic myopathy.

†See Table 1.

‡The number of CTG repeats for both alleles in one patient of each family.

Mental Retardation

One patient (patient 13-2) had mental retardation of unknown cause since infancy. His only muscle findings were noted on an electromyographic study that revealed myotonic discharges. On examination at 18 years of age, he was found to have cataracts, typical in appearance to those in DM. None of the 26 other patients who were examined had any mental disturbances.

LABORATORY STUDIES

Blood Studies

Serum creatine kinase was abnormally elevated in 17 of the 25 patients tested (Table 1). Two patients had episodes of dark urine associated with muscle pain, and one of the two patients had transient renal insufficiency. These episodes occurred after unusual athletic activity on two occasions in one patient (patient 14-1) and a few days after minor surgery in another patient (patient 12-1). The actual creatine kinase levels during these episodes are unknown. A year or more later, creatine kinase levels in patient 14-1 were 569, 320, and 2800 U/L, and in patient 12-1 they were 620, 240, and 1120 U/L. Fourteen of 18 patients tested had elevated levels of γ-glutamyltransferase, while the levels of alanine aminotransaminase and aspartate aminotransaminase were either normal or borderline (Table 1). None of these patients had a history of alcohol abuse or of other problems that predispose to liver disease.

Muscle Computed Tomographic Scans

Four patients with proximal leg weakness (patients 3-1, 5-1, 6-1, and 9-1) underwent computed tomographic scans of their thighs. No signs of atrophy or of structural damage were seen.

Table 3. Similarities and Differences Between DM and PROMM*

	DM	PROMM
Core features		
Myotonia	+	+
Cataract	+	+
Muscle weakness	+	+
Localization of muscle weakness		
Facial weakness, jaw muscles	++	–
Distal limb muscle weakness	++	–
Proximal leg muscle weakness	(+)	++
Sternocleidomastoid muscle	+	+
Muscle symptoms		
Muscular atrophy	++	(+)
Muscle pain	–	+
Variation in muscle strength	–	+
Heart		
Cardiac arrhythmias	++	+
Liver		
γ-Glutamyltransferase elevation	+	+
Brain		
Late change in mental state	+	–
Hypersomnia	+	–
DNA		
CTG repeat enlargement of the DM gene locus	+	–
Anticipation	+	?
Congenital type disorder	+	?

*DM indicates myotonic dystrophy; PROMM, proximal myotonic myopathy; plus sign, present; two plus signs, present and very prominent; plus sign in parentheses, present but to only a minor degree; minus sign, not present; and question mark, not yet known whether the finding occurs or does not occur.

Muscle Morphology

The histochemical findings were remarkably similar among the nine biopsy specimens. In general, the appearance was that of a nonspecific myopathy. There was a mild to moderate increase in central nuclei, and there was hypertrophy, mainly of type 2 fibers. There were no ring-binden or subsarcolemmal masses, and there was no selective atrophy of type 1 fibers. No inflammatory cell infiltrates were seen, and there was no increase in connective tissue. Scattered small atrophic fibers, similar to the changes in early denervation, were observed in eight of the nine biopsy samples. The significance of these findings was unclear in view of the absence of fiber type grouping or other signs of chronic denervation. Electron microscopy revealed only nonspecific changes.

DNA Analysis

In all patients, leukocyte DNA analysis revealed normal *Eco*RI and *Bgl*I DNA fragments, without abnormal expansion of the DM gene. The sizes of the CTG repeat of the DM gene in leukocyte DNA for one patient in each of the 14 families are shown in Table 2. The CTG repeat sizes were identical in DNA isolated from muscle tissue and leukocytes in the three patients (patients 1-1, 6-1, and 10-1) who had DNA analyzed from both tissue specimens.

In Vitro Investigations of Muscle Fiber Bundles

In vitro studies of case 7-1 have been described as case MYD-13 by Franke et al.[12] His muscle fibers had normal resting membrane potential, a normal steady-state current voltage relationship, and a normal chloride conductance. Myotonic discharges were recorded in these muscle fibers in vitro.

COMMENT

The clinical and laboratory findings in the 14 families described herein provide a picture of the characteristic features of PROMM.[2] Knowing about these features makes it easier to identify the similarities and differences between PROMM and DM. It is apparent that PROMM is a multisystem disease, like DM,[15,16] with abnormalities of the skeletal muscle, lens, heart, and liver (**Table 3**). It is likely that other organ systems may also be involved.[1] Proximal myotonic myopathy has certain unique differences compared with DM. Unlike DM, there is proximal, rather than distal, weakness and sparing of the facial muscles, and patients with PROMM have no abnormal expansion of the CTG repeat in the DM gene,[1,2] which is the hallmark of DM.[3-5] Moreover, DNA analysis in three families has shown no linkage to the DM locus (or to the loci for paramyotonia or myotonia congenita). Therefore, another gene locus must be involved.[2]

There are certain practical implications to the clinician. If a patient has certain features usually seen in DM and does not have an abnormal trinucleotide repeat expansion in the DM gene, this does not necessarily indicate that the patient has one of the above-mentioned benign myotonic disorders. The patient may have PROMM, and, while the complications of this disorder apparently are somewhat less severe than those in myotonic dystrophy, patients with PROMM can develop cataracts and cardiac conduction disturbances, which are important issues in management.

Some patients with PROMM may come to the clinician with a relatively unique set of complaints, which include a variation in weakness over days or even weeks, and sometimes an unusual burning, tearing pain in their muscles. The underlying mechanisms are unknown. It is of interest that two patients had episodes suggestive of rhabdomyolysis and both had elevations of creatine kinase levels that were higher than those in the other patients with PROMM. These features may mislead the clinician. It is important to consider myotonia and to look for it. Establishing the diagnosis of PROMM, as opposed to DM, appears to have a more favorable long-term prognosis. Up to the present, none of the patients with PROMM have shown a late deterioration in mental status, hypersomnia, dysarthria, dysphagia, respiratory failure, or other pulmonary complications that occur in DM. However, a note of caution is necessary. As more families with PROMM are evaluated, it is possible that individuals with more severe weakness, more apparent muscular atrophy, and more extensive involvement of other organ systems will be identified.

Other care issues, such as genetic counseling, will become important. Seven of the 11 parent-child pairs in

this article showed earlier onset and more severe disease in the child, a pattern that raises the possibility of anticipation in families with PROMM. Another important issue is whether a congenital form of this disorder exists. Two patients with PROMM have been observed with mental retardation since early childhood.[2] This could be an incidental occurrence. Further studies of other families with PROMM are necessary to search for clinical evidence of anticipation, as well as a congenital form of the illness.

ELECTROPHYSIOLOGIC IN VITRO studies of muscle fibers in two patients with PROMM[2,12] confirmed that the myotonia originates in the muscle fiber. The conventional EMG reveals "typical" myotonic discharges. However, in some patients complex discharges and very rapid spike discharges with a frequency of over 200 Hz (similar to that in neuromyotonia) can be seen. The histologic appearance of muscle tissue specimens reveals scattered highly atrophic single fibers. These findings might occur as a result of lesions in the distal branches of some motor neurons.

A few patients with PROMM experienced variation in their degree of weakness, and exercise clearly improved their muscle strength for a short period of time, lasting up to half an hour. A somewhat similar phenomenon has been observed in patients with recessive chloride channel myotonia.[17] However, in vitro analysis of muscle fiber membrane parameters in two patients with PROMM showed a normal chloride conductance,[2,12] in contrast to findings in the recessive type of chloride channel myotonia.[18] The same studies also showed a normal resting membrane potential in muscle fibers of the patients with PROMM, in contrast to those with DM with an abnormally low resting potential.[12,15]

Proximal myotonic myopathy and DM are two distinct autosomal dominant disorders with different gene loci. The DM gene locus is on chromosome 19.[3-5] The gene locus for PROMM is not yet known. The DM locus has been excluded in three of the families with PROMM.[2] The clinical characteristics of the 35 patients from the 14 families described in this article are identical to those in the patients whom we have described previously,[2] and we believe that all of these families have PROMM. However, it is necessary to mention that while the phenotype of PROMM in the 14 families described in this article is homogeneous, we cannot exclude the possibility that the PROMM phenotype is caused by genetic locus heterogeneity (eg, different gene loci for PROMM). The pedigree structure of these 14 families was not sufficient to permit linkage analysis. In our review of the literature related to DM and other myotonic disorders,[19,20] we have found no descriptions of families with the clinical features of PROMM. At present, there are no detailed clinical description of families having the PROMM phenotype that also have an abnormal enlargement of the CTG repeat of the DM gene. However, it is interesting to note a recent article that mentions one patient with a clinical appearance that resembles that of patients with PROMM and who has an abnormal enlargement of the DM gene.[21] Researchers and clinicians have also wondered if, on rare occasions, DM may result from point mutations or deletions within the DM gene. To date, examples of such mutations in the gene and a description of the clinical phenotype have not appeared.

The DM gene on chromosome 19 codes for a serine threonine kinase,[3-5] but the function of the DM kinase and its potential role in the pathomechanism of DM are unknown. It is interesting to consider that both DM and PROMM share certain common findings, and this might indicate that both of these disorders have a final common pathway involved in their pathophysiology. For example, the cataracts observed in patients with PROMM are virtually identical to those observed in DM, showing posterior capsular lens opacities with a colorful, iridescent appearance.[22,23] Another example is the hepatic dysfunction evidenced in both DM and PROMM by an elevation of serum γ-glutamyltransferase.[24,25] The pathomechanism responsible for either of these alterations in function is not known.

The most obvious example of a final common pathway in PROMM and DM is the presence of myotonia and weakness in both conditions. On the other hand, the lack of substantial atrophy in patients with PROMM is in contrast to the sometimes profound muscular atrophy in DM. There must be certain unique factors accounting for this difference between PROMM and DM. Discovering the gene lesion in PROMM and identifying its gene product will help to extend our understanding of the pathophysiology in DM and the role of the DM kinase.

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