150 mg 2 to 3 times daily, which resulted in noticeable improvement in diplopia and ptosis.

Ocular findings can occur in myotonia congenita, although they are reported rarely. This is a unique description of a patient with a *CLCN1* gene mutation who presented with fluctuating diplopia, ocular misalignment, and ptosis as initial symptoms of myotonia congenita. This patient's response to mexilitine suggests myotonia of the extraocular muscles as the likely mechanism for her symptoms. MC is an important diagnostic consideration in evaluating patients with fluctuating ocular symptoms.

Karen Odrzywolski, MD

Nicholas E. Johnson, MD

Paul T. Twydell, DO

Department of Neurology, University of Rochester Medical Center, Rochester, New York

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CASE STUDY OF SPORADIC MITOCHONDRIAL DISEASE WITH MYOTONIC DISCHARGES AND OPTIC ATROPHY

A 44-year-old woman presented with a 6-year history of progressive bilateral ptosis and muscle weakness. Family history was unremarkable. Neurological examination revealed decreased visual acuity, bilateral ptosis and restriction of eye movements during upgaze, downgaze, and adduction. Bilateral optic atrophy and normal appearing retinae were observed (Fig. 1A). She had normal proximal muscle strength and tendon reflexes, and there was no action or percussion myotonia. Cranial and orbital MRI, electrocardiography, echocardiography, routine blood chemistry, hemogram, serum creatine kinase, cerebrospinal fluid (CSF) examination, and serum and CSF lactate:pyruvate ratio were normal. Needle electromyographic (EMG) examination showed myotonic discharges and polyphasic, short duration motor unit potentials with full recruitment (Fig. 1B). Motor and sensory conduction and repetitive nerve stimulation studies were normal. Muscle biopsy of the deltoid muscle showed cytochrome oxidase negative fibers with ragged-red fibers that stained intensely blue with the histochemical reaction for succinate dehydrogenase (Fig. 1C and D).

According to her clinical, EMG, and muscle biopsy findings chronic progressive external ophthalmoplegia (CPEO) was considered as a possible diagnosis. Analysis of *OPA1* and *RRM2B* genes by means of direct sequencing and multiplex ligation-dependent probe amplification (MLPA) analysis showed normal results. The 3 primary Leber hereditary optic neuropathy (LHON) mutations were excluded. No mtDNA deletion was found in long range polymerase chain reaction and Southern blot studies.

A single pathogenic mutation, c.803 G>C, p.Gly268 Ala heterozygous, was detected in *POLG1*. It was described as pathogenic in the compound heterozygous state with another mutation (recessive pattern of inheritance).[1–3] Deletions or duplications of the *POLG1* gene were excluded by means of MLPA analysis. In DNA from muscle of the patient, the variant m.16023 C>T was found with a high heteroplasmy rate of 90–95%. This variant was not detected in blood DNA of the patient. The position m.16023 is the first, 5′-terminal nucleotide of the mitochondrial tRNA proline, located in the acceptor stem of the tRNA.[4] A mutation in this region of the tRNA might perhaps cause disease, as position 1 of the mt-tRNA Pro is a highly conserved nucleotide.[5]

Myotonic discharges may occur with or without clinical myotonia in myotonia congenita, paramyotonia, myotonic dystrophy, polymyositis, acid maltase deficiency (Pompe disease), hyperkalemic periodic paralysis, and myotubular myopathy.[6] Our patient had neither clinical nor pathological features of these diseases. Therefore, both the ophthalmoplegic myopathy and myotonia could be explained by mitochondrial pathology in our patient. This clinical picture is further complicated by optic atrophy, which is a hallmark of LHON, but not CPEO.

The mitochondrial diseases have clinical variability, and there is poor correlation between genotype and phenotype. For this reason, classification of these diseases is complex.[7–10] Our patient shows a sequence variant, m.16023C>T, in the highly conserved position 1 of the acceptor stem of the mitochondrial tRNA Pro, but only in muscle DNA, not in blood DNA. Therefore, this variant might be the cause of the symptoms of the patient, but for further conclusions, her family members have to be analyzed.

To date, myotonic discharges in mitochondrial disorders have been reported only in 1 case.[11] Our findings provide further evidence that myotonic discharges can be part of the clinical spectrum of mitochondrial disease.

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Aysun Soysal, Assist. Prof[1]

Burcu Yüksel, MD[1]

Birgit Czermin, PhD[2]

Selcen Aydemir, MD[1]

Betül Tuğcu, MD[3]

Fikret Aysal, MD[1]

Baki Arpaci, Assist. Prof[1]

[1]Department of Neurology, Bakirkoy Research and Training Hospital for Psychiatry, Neurology and Neurosurgery, Istanbul, Turkey

[2]Medical Genetic Center, Munich, Germany

[3]Department of Ophthalmology, Bakirkoy Dr. Sadi Konuk Research and Training Hospital, Istanbul, Turkey

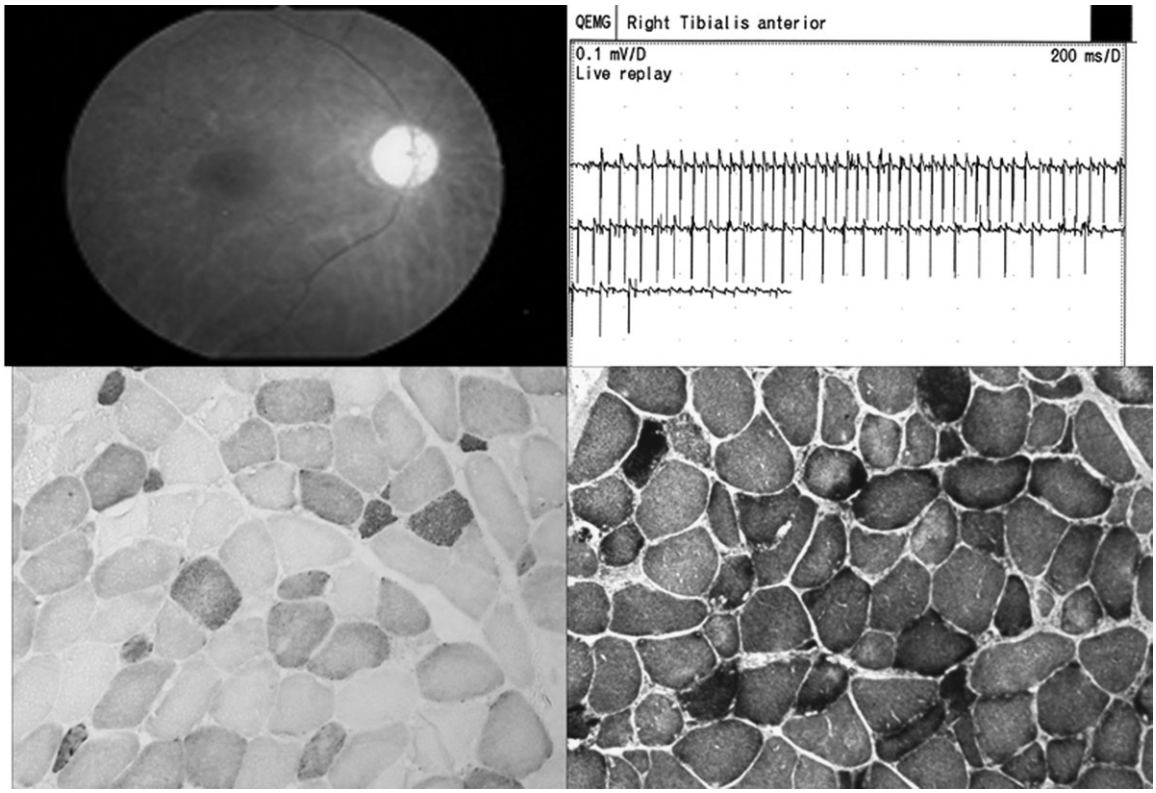

FIGURE 1. Funduscopic examination, EMG findings and muscle biopsy of the patient. A: Optic atrophy of the right eye. B: Myotonic discharges in the right tibialis anterior muscle. C: Cytochrome oxidase (COX) negative fibers accompanied with ragged-red fibers (RRF). D: The histochemical reaction for succinate dehydrogenase (SDH) stains intensely blue on deltoid muscle biopsy. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

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