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CASE REPORT

A Patient with Myotonic Dystrophy Type 1 Presenting as Parkinsonism

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ABSTRACT

The current body of literature contains 5 reports of myotonic dystrophy (DM) with parkinsonism: 4 reports of DM type 2 and 1 report of clinically suspected DM type 1. To date, there have been no genetically proven cases of DM type 1 with parkinsonism. Here, we report the first case of genetically proven DM type 1 and parkinsonism that developed ahead of muscle symptoms with bilateral putaminal, presynaptic dopaminergic deficits on imaging. A 54-year-old female patient presented with bradykinesia, axial and bilateral limb rigidity, stooped posture, and hypomimia, which did not respond to levodopa. At age 56, she developed neck flexion weakness. Examination showed bilateral facial weakness, percussion and grip myotonia, and electromyography confirmed myotonic discharges. A genetic study of DM type 1 showed a *DMPK* mutation. At age 58, gait freezing, postural instability, and frequent falling developed and did not respond to increasing doses of levodopa. At age 59, the patient died from asphyxia.

Key Words Parkinsonism; parkinsonian disorders; myotonic dystrophies; myotonic dystrophy 1.

Myotonic dystrophy (DM) is a genetic disorder that causes both muscle dystrophy and myotonia in combination with multisystem involvement of the eye, heart, endocrine system, and central nervous system. DM is a genetic disorder classified as type 1 or type 2. DM type 1 is phenotypically more severe than DM type 2.[1] In DM type 1, symptoms include ocular cataracts, cardiac conduction defects, insulin resistance, hypothyroidism, hypogonadism, infertility, constipation, and diarrhea.[1] A variety of mental disorders are seen, such as mental slowness, memory disturbances, indifference, apathy, lack of spontaneity, difficulties in performing frontal lobe tasks and visual-spatial cognitive tasks, excessive daytime sleepiness and mood changes.[1] DM type 1 is caused by a $(CTG)_n$ microsatellite repeat expansion in the untranslated 3' region of the dystrophin myotonin protein kinase (*DMPK*) gene in chromosome 19q13.3, whereas type 2 is due to a $(CCTG)_n$ expansion in intron 1 of the nucleic acid-binding protein (CNBP) gene in chromosome 3q21.3.[1] Since 1996, there have been 5 reports of DM with parkinsonism: 4 reports of DM type 2 and 1 report of clinically suspected DM type 1 (Table 1).[2-6] There have been no genetically proven cases of DM type 1 with parkinsonism. Clinical signs of parkinsonism, severity, and levodopa response were variable in these 5 reported cases. Four of the 5 previous cases presented with myotonia first and subsequently developed parkinsonian features, and only 1 case developed parkinsonism ahead of muscle symptoms (Table 1). Here, we report the first case of DM type 1 with *DMPK* mutations presenting with parkinsonian syndrome and bilateral putaminal, presynaptic dopaminergic deficits on dopamine transporter (DAT) imaging.

CASE REPORT

A 54-year-old female presented with complaints of a one-year history of uncomfortable range of motion in all four limbs

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Table 1. Summary of patients with DM and parkinsonism

Authors	Patients		DM features			Parkinsonian features		
	Age (yrs)	Sex	Gene test for DM	Diagnosed DM type	Onset age of muscle involvement (yrs)	Onset age of parkinsonism (yrs)	Parkinsonism	Levodopa response for parkinsonism
Okuma et al.[2]	63	F	Not performed	Type 1	40	50	Asymmetric tremor, small step with freezing, bradykinesia, postural instability and hypomimia	Good response
Hund et al.[3]	59	F	DM type 2 gene positive	Type 2	50	52	Stooped posture, hypomimia and low voice	Good response
Chu et al.[4]	65	M	DM type 1 gene negative, not performed for type 2	Type 2	55	63	Asymmetrical tremor, rigidity, bradykinesia, hypomimia, stooped posture, and gait disturbance	Partial response
Celik et al.[5]	41	F	Not performed	Type 2	38	40	Bilateral resting tremor, rigidity, bradykinesia and hypomimia	Good response
Annic et al.[6]	47	F	DM type 2 gene positive	Type 2	51	47	Bilateral tremor, bradykinesia, rigidity and gait disturbance	Partial response
Current case	54	F	DM type 1 gene positive	Type 1	56	53	Bilateral bradykinesia, rigidity, stooped posture, hypomimia, gait freezing and postural instability	Minimal response

DM: myotonic dystrophy.

with stiffness and slowness while moving and walking, and she had no significant history of prior illness or medication. Family history revealed that one of her three siblings experienced a cerebral infarction at the age of 52, and her mother was diagnosed with dementia at the age of 90. On initial examination at age 54, the patient demonstrated hypomimia, mild to moderate bilateral bradykinesia on finger tapping, hand-grasp, and pronation-supination movements of the hands, mild axial and bilateral limb rigidity, mildly stooped posture, and slowing gait with bilaterally reduced arm swing, though no resting or kinetic tremor. Eye movements showed breaking up of smooth pursuit but no supranuclear gaze palsy. Autonomic symptoms and signs were not evident. She did not have depression, sleep problems, or loss of smell. Her Mini-Mental State Examination score was 29/30. The Frontal Assessment Battery score was 15/18, which suggested mild frontal lobe dysfunction. MRI of the brain showed mild diffuse cerebral atrophy. Serum copper and ceruloplasmin tests for Wilson disease were within the normal ranges. A levodopa trial showed subjective minimal improvement. The initial diagnosis was atypical parkinsonian syndrome based on bilateral symmetric parkinsonian features and poor levodopa response. DAT imaging using an (18)F-FP-CIT [(18)F-fluorinated N-3-fluoropropyl-2-beta-carboxymethoxy-3-beta-(4-iodophenyl) nortropane] positron emission tomography scan showed moderately to severely decreased uptake in the putamen bilaterally (Figure 1). At age 56, she developed difficulties raising her head up when lying on her back. Examination showed neck flexion weakness, mild bilateral facial weakness, and percussion and grip myotonia. Needle electromyography confirmed myotonic discharges in proximal and distal muscles. Ophthalmologic examination showed bilateral cataracts. Echocardiogra-

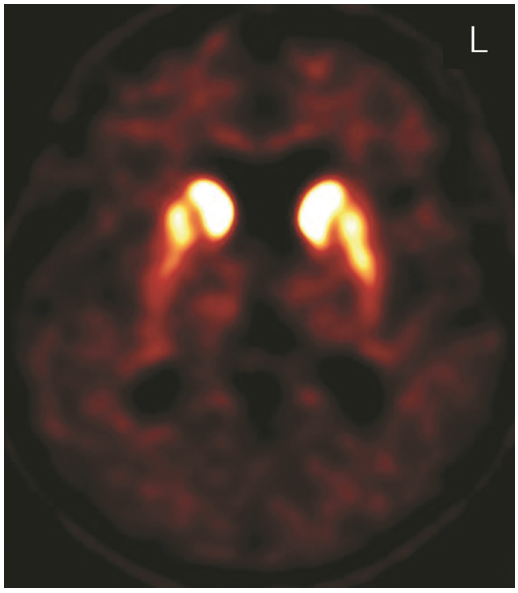

Figure 1. FP-CIT positron emission tomography scan showed moderately to severely decreased uptake in the putamen bilaterally.

phy and electrocardiography were normal. A genetic screen for DM type 1 showed an abnormal CTG repeat length with 120 repeats in the untranslated 3' region of *DMPK* on chromosome 19q13.3. By age 58, the patient had developed gait freezing, postural instability, and frequent falling, as well as progressed to moderate to severe bilateral bradykinesia on finger tapping, hand-grasp, and pronation-supination movements of the hands, moderate to severe axial and bilateral limb rigidity, and moderate stooped posture. Increasing her dose of levodopa to 1,300 mg per day was not effective. She developed dysarthria, dysphasia, and severe weight loss. At age 59, she died from asphyxia. An autopsy was not performed.

DISCUSSION

In this report, the patient was initially diagnosed with atypical parkinsonian syndrome based on bilateral symmetric parkinsonian features and a poor levodopa response. DAT imaging confirmed the presynaptic dopaminergic deficits in the bilateral putamen. Later, she was diagnosed with DM type 1 based on myotonia clinical manifestations and *DMPK* mutations. To date, there have been no reports of genetically proven cases of DM type 1 with parkinsonism. To our knowledge, this is the first reported case of DM type 1 with *DMPK* mutations and parkinsonism that developed ahead of muscle symptoms with bilateral putaminal, presynaptic dopaminergic deficits on DAT imaging. The prevalence of DM type 1 appears to be more common than DM type 2, except in Germany, Poland, and Finland, where DM type 2 is as common as DM type 1.[1] However, parkinsonism has been reported more often in DM type 2 cases than in type 1 cases (Table 1).

Of the previous 5 reported patients with DM who developed parkinsonism (Table 1), an autopsy was performed on 1 patient with clinically diagnosed DM type 1 and parkinsonism,[2] who was never genetically tested. The autopsy in the patient showed marked cell loss and Lewy bodies in the substantia nigra (SN) and diffuse myelin loss in the cerebral white matter.[2] However, Lewy bodies in the SN have been reported in other patients with genetically proven or clinically diagnosed DM without parkinsonism.[7] Other neuropathological changes found upon autopsy of genetically proven or clinically diagnosed DM included neurofibrillary tangles, observed mostly in the hippocampus and the temporal neocortex.[8] Marinesco bodies and neuronal loss of the medullary arcuate nucleus and reticular formation were also noted in some cases,[9] but were not found consistently, nor were clinicopathological features consistent. Other neuropathological findings included intracytoplasmic inclusion bodies in the thalamus, SN, cerebral cortex, caudate nucleus, and putamen,[10] of which the mechanism of pathology remains unknown. Lewy bodies and intracytoplasmic inclusion bodies found in the SN or the subcortical striatum may raise the possibility of association between parkinsonism and DM, but it warrants further studies.

In conclusion, parkinsonism has been reported in patients with DM. The association of parkinsonism and DM may not be coincidental given the current case and other similar reports and their neuropathology results. However, further research is needed to understand the relationship between parkinsonism symptoms and DM.

Conflicts of Interest

The authors have no financial conflicts of interest.

Acknowledgments

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