A Mutation In Neurodegeneration With Brain Iron Accumulation – Two Brothers

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ICNC 2022
17th INTERNATIONAL CHILD NEUROLOGY CONGRESS
ANTALYA, TURKEY | OCTOBER 3-7, 2022

INTRODUCTION

Mitochondrial membrane protein-associated neurodegeneration (MPAN) is an inherited disorder caused by a mutation in the C19orf12 gene, characterized by basal ganglia involvement with various neurological and psychiatric symptoms. MPAN typically presents with progressive dystonia-parkinsonism, optic atrophy, axonal motor neuronopathy, and iron accumulation in the globus pallidus and substantia nigra in childhood or adolescence.

CASE 1

A ten-year-old boy was presented with behavior complaints, gait disturbances, and vision loss. He had toe walking since the age of seven, nail-biting, lack of attention, and impaired speech since the age of eight. He was born to healthy consanguineous parents. His developmental stages were normal until seven years of age. His visual acuity decreased (0.2 on the right, 0.2 on the left), the optic disc was bilaterally pale, and it was compatible with optic atrophy (Figure I). Other findings were spasticity of legs, tip toe walking, increased deep tendon reflexes, bilateral pes cavus, and bilateral Babinski sign. Sensory examination was normal. The gait pattern was fingertip. WISCR; (verbal score 90, performance score 82, general score 86) was normal. Electromyography (EMG), echocardiography (ECHO), electrocardiography (ECG) were normal. Brain magnetic resonance imaging (MRI) showed signal changes due to iron accumulation in bilateral substantia nigra, red nucleus, globus pallidus, dentate nucleus, and bilateral optic nerve atrophy (Figure I). With next-generation sequencing analysis the c.194-2A>G variant was found to be homozygous in the 2nd intron of the C19orf12 gene. In the segregation of the family, it was determined that his mother, his father, and 19-year-old brother were carriers, his 21-year-old sister was healthy and his 8.5-year-old brother was carrying the same variant (Case 2).

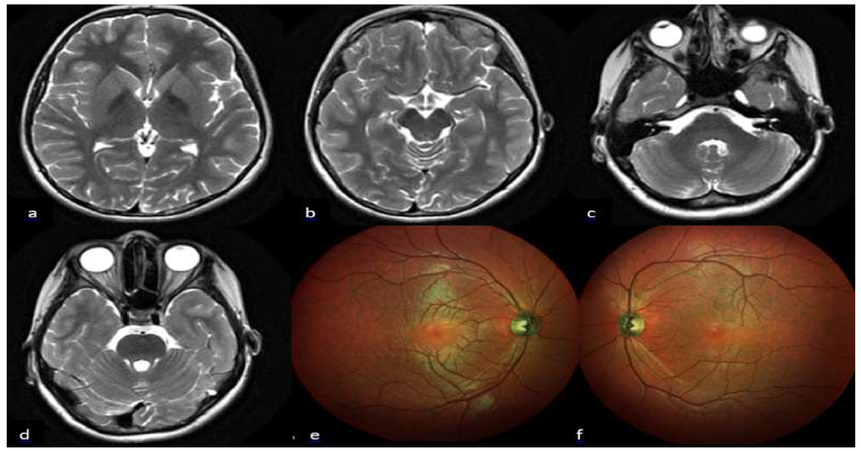

Figure I. Cranial magnetic resonance imaging of Case 1, hypointensities in the globus pallidus (a), substantia nigra, red nucleus (b) and dentate nucleus (c), thinning of the optic nerves (d) on T2 weighted images. Optic atrophy on the right (e) and left (f) fundus photography.

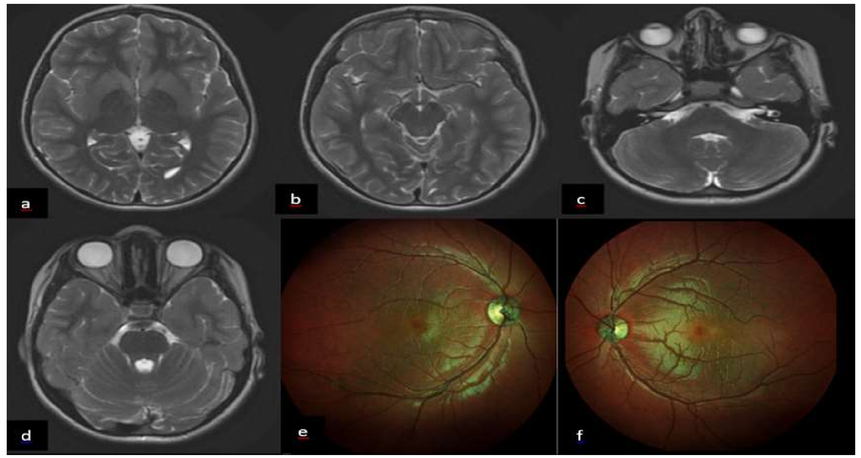

Figure II. Cranial magnetic resonance imaging of Case 2, hypointensities in the globus pallidus (a), substantia nigra, red nucleus (b), and dentate nucleus (c), thinning of the optic nerves (d) on T2 weighted images. Optic atrophy on the right (e) and left (f) fundus photograph.

CASE 2

An eight-and-a-half-year-old boy complained of visual loss and behavioral disturbance. He was born at 32 weeks, 2500 g by vaginal delivery, and his developmental stages were normal until he was five years old. At the age of five, it was noticed that he had aggression, not being able to control his emotions, and at the age of seven, he had vision problems. His visual acuity was found to decreased (0.2 on the right, 0.2 on the left), and the optic disc was pale bilaterally (Figure II). He had bilateral pes cavus. His deep tendon reflexes were hyperactive in the lower extremity. Sensory examination was normal. WISCR test (verbal score 108, performance score 82, overall score 95) , EMG, ECHO, ECG were normal. His brain MRI showed signal changes due to iron accumulation in bilateral substantia nigra, red nucleus, globus pallidus, and dentate nucleus, and bilateral optic nerve atrophy (Figure II). C19orf12 gene mutation was detected.

CONCLUSION

Cognitive decline, neuropsychiatric findings, and dementia are characteristic of MPAN. It is critically important to question the progressive nature of accompanying vision and related gait problems in patients followed by psychiatry with the diagnosis of attention deficit, behavioral change, and mood disorder. In the presence of spasticity, neuropsychiatric findings, visual problems in early childhood and iron accumulation in the globus pallidus and substantia nigra in MRI, MPAN disease, one of the early-onset forms of NBIA group diseases, should be considered.

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