Mitochondrial Membrane Protein-associated Neurodegeneration due to Novel Homozygous Mutation in the C19orf12 Gene

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A 16-year-old-boy born to non-consanguineous parents presented with slowly progressive cognitive decline and gait disturbance for the past 4 years. The gait disturbance was started in the form of frequent falls and intermittent twisting of bilateral lower limbs. Subsequently, he developed excessive talking, forgetfulness, and slow speech. Currently, he was able to walk but unable to run, jump or skip. There was no history of diurnal variations, seizures, and family history was unremarkable. Examination revealed moderate intellectual disability (intelligence quotient: 49), bilateral optic atrophy, dysarthria, bradykinesia, intermittent generalized dystonia, tremors, and bilateral striatal toes. Magnetic resonance imaging (MRI) of the brain showed mineral deposition in basal ganglia [Figure 1]. A next-generation sequencing revealed a novel homozygous pathogenic variant in the C19orf12 gene (c.196G>T; p.Gly66Trp), confirming the diagnosis of mitochondrial membrane protein-associated neurodegeneration.

Mitochondrial membrane protein-associated neurodegeneration (MPAN) is the third most common form of NBIA, caused by a homozygous or compound heterozygous mutation in the C19orf12 gene. The age of onset ranges from 3 years to 30 years and characteristic clinical features are extrapyramidal and pyramidal signs, neuropsychiatric problems, vision impairment, dysarthria, and sometimes axonal neuropathy.[1] The MRI features of MPAN are iron deposition in substantia nigra and globus pallidum without an eye of tiger appearance (characteristic of Pantothenate kinase-associated neurodegeneration) on T2-weighted sequences.[1,2] Linear

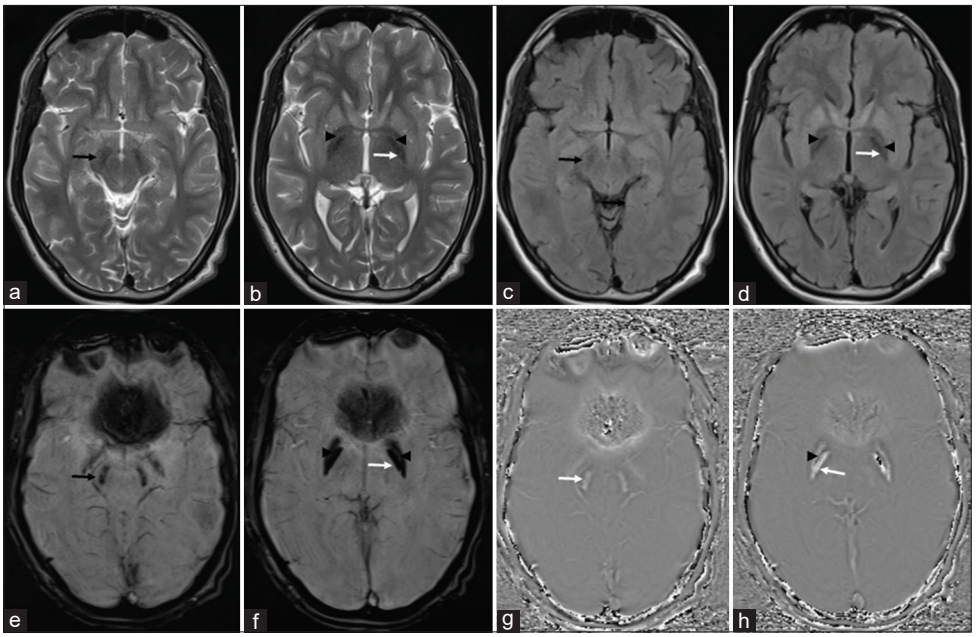

Figure 1: Magnetic resonance imaging of the brain. T2-weighted (a, b) and FLAIR (c, d) axial images showing symmetrical hypointense signal changes in the bilateral substantia nigra (a, c; black arrow) and globus pallidum (b, d; white arrow) with a linear hyperintense streak in the medial medullary lamina, between the globus pallidi internus and globus pallidi externus (b, d; arrowhead). These images also demonstrate bilateral and symmetrical hyperintense signal changes in caudate and putamen. Susceptibility-weighted (e, f) axial sequences show bilateral hypointense signal changes in the substantia nigra (black arrow) and globus pallidus (white arrow) with a hyperintense streak in the medial medullary lamina (arrowhead). These signals are hyperintense (g, h; white arrow) on filtered phase sequences with a medial streak of hypointense signal changes (h; arrowhead)

streak-like involvement of medial medullary lamina of globus pallidi is striking. Cerebral and cerebellar atrophy can be seen with advanced disease.[3]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Submitted: 17-Jun-2020 **Revised:** 17-Jun-2020 **Accepted:** 17-Jun-2020
Published: 08-Jan-2021

DOI: 10.4103/aian.AIAN_620_20