Characteristic MRI findings in beta-propeller protein-associated neurodegeneration (BPAN)

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A 31-year-old woman presented with severe dystonia-parkinsonism. She had nonprogressive psychomotor retardation and cognitive dysfunction from childhood without evidence of dystonia or parkinsonism. At age 30, she then developed severe dystonia and gait disturbance. There was neither dystonia nor parkinsonism before age 30. MRI revealed cerebral atrophy and iron accumulation in the globus pallidus and substantia nigra (figure 1, A–D). The characteristic MRI findings were hyperintensity of the substantia nigra with a central band of hypointensity in T1-weighted axial slices (figure 1, B). Beta-propeller protein-associated neurodegeneration (BPAN) was diagnosed based on MRI findings and identification of a novel heterozygous mutation in the *WDR45* gene (NM_007075.3: c.519+1_519+3del) (figure 2). This is a neurodegeneration involving brain iron accumulation (NBIA) characterized by psychomotor retardation from childhood and dystonia-parkinsonism in midadulthood.^{1,2} Although we could not analyze the father's gene since he had died, the mother had no mutation in the *WDR45* gene (figure 2). Thus, it might be a de novo mutation in the *WDR45* gene, as reported previously.^{1,2}

L-Dopa/decarboxylase inhibitor treatment (200 mg/day orally) led to improvement of the rigidity and bradykinesia in our patient. She became able to move by herself by crawling on her hands and knees and no longer needed meal assistance. In addition, she became able to utter a few words like “thanks” and “bye,” although the dystonia of the lower limbs remained unchanged. Since T1-weighted hyperintensity of the substantia nigra with a central band of hypointensity has not been found in other NBIA disorders, including neuroferritinopathy,

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Figure 1 Brain MRI findings in the patient

(A, B) T2-weighted MRI shows marked hypointensity in the globus pallidus and substantia nigra in axial slices. (C) T1-weighted MRI shows hyperintensity of the substantia nigra with a central band of hypointensity in an axial slice (arrows). (D) T1-weighted MRI shows cerebral atrophy and hyperintensity of the substantia nigra (arrowhead) in a sagittal slice.

Figure 2 Identification of a novel heterozygous mutation in the *WDR45* gene

Electropherograms of the patient and her mother using a forward primer are shown. A novel heterozygous mutation (NM_007075.3: c.519+1_519+3del, underlined), which may result in abnormal splicing, was identified in intron 8 (splice donor site) of the *WDR45* gene in the patient, as shown by the double signals due to the 3 bp deletion. Meanwhile, the mother had no mutation in the *WDR45* gene. The colored peaks denote nucleotide bases as follows: black, guanine; red, thymine; blue, cytosine; and green, adenine.

aceruloplasminemia, and pantothenate kinase-associated neurodegeneration, this finding should facilitate the diagnosis of BPAN.

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