'Comb Sign': A Novel Appearance of Substantia Nigra in Mitochondrial Membrane Protein-Associated Neurodegeneration

Divyani Garg, Ayush Agarwal, Ajay Garg[1], Roopa Rajan, Achal Kumar Srivastava

Departments of Neurology and [1]Neuroradiology, All India Institute of Medical Sciences, New Delhi, India

Mitochondrial membrane protein-associated neurodegeneration (MPAN)[1] is characterized by progressive spasticity, gait abnormalities, dystonia, cognitive decline, neuropsychiatric abnormalities, and variably, optic atrophy, axonal peripheral neuropathy, and parkinsonism. It is attributed to biallelic or rarely heterozygous pathogenic variants in the *C19orf12* gene. Magnetic resonance brain (MRI) brain is defined by iron accumulation in the globus pallidus and substantia nigra (SN),[2] and isointense streaking of the medial medullary lamina separating the hypointense globus pallidus externa and interna, referred to as the "split pallidum" sign. Rarely, the "eye of the tiger" sign has also been reported in MPAN.

We report a new radiological observation in four patients with genetically proven MPAN (homozygous pathogenic mutation [c.166delG, c.199delG, c.163G>T] on exon 3 of the *C19orf12* gene) who demonstrated the presence of a peculiar appearance of the substantia nigra on quantitative susceptibility-weighted imaging. This showed a "comb-like" appearance of the SN on the ventral aspect [Figures 1 and 2]. We hypothesize that the horizontal band and teeth are formed by iron deposition in the SN and descending corticospinal tracts, respectively, resembling a "comb." The corticospinal tract involvement might explain the prominent spasticity observed in MPAN patients. We have not observed this finding in any other form of NBIA, and propose this as a novel radiological indicator of MPAN.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

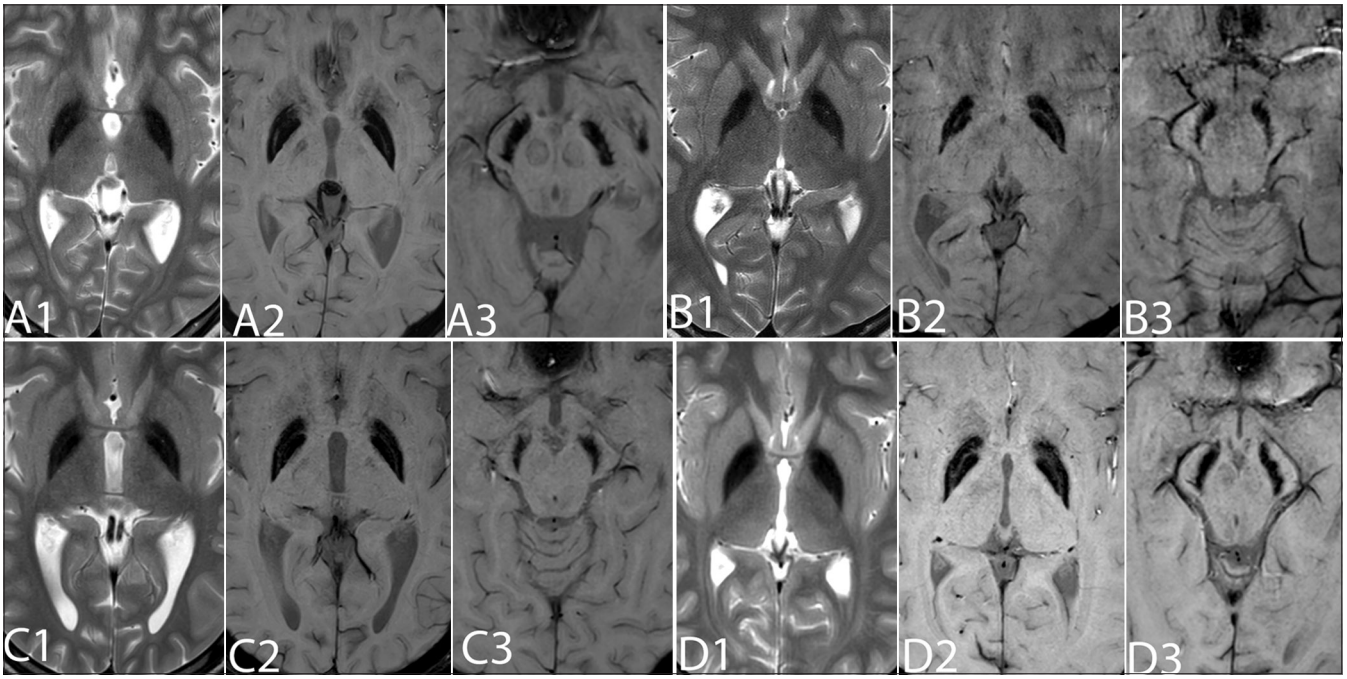

Figure 1: MRI scans of four MPAN patients (A-D). Axial T2 (A1, B1, C1, and D1) and SWI (A2, B2, C2, and D2) at the level of basal ganglia show isointense streaking of the medial medullary lamina between the hypointense globus pallidus interna and the externa. SWI (A3, B3, C3, and D3) at the level of substantia nigra ganglia show "streaky" anterior border of the substantia nigra with brush-like linear hypointensities extending anteriorly into the cerebral peduncle: "comb sign"

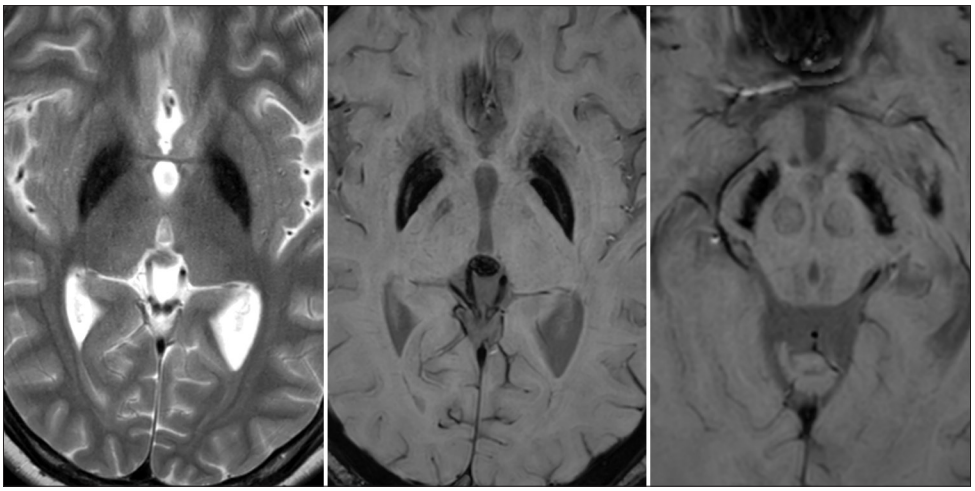

Figure 2: Zoomed-in MRI image of one of our MPAN patients, highlighting the changes mentioned in Figure 1

References

1. Hogarth P, Gregory A, Kruer MC, Sanford L, Wagoner W, Natowicz MR, *et al.* New NBIA subtype: Genetic, clinical, pathologic, and radiographic features of MPAN. Neurology 2013;80:268-75.
2. Dusek P, Mekle R, Skowronska M, Acosta-Cabronero J, Huelnhagen T, Robinson SD, *et al.* Brain iron and metabolic abnormalities in C19orf12 mutation carriers: A 7.0 tesla MRI study in mitochondrial membrane protein-associated neurodegeneration. Mov Disord 2020;35:142-50.

Address for correspondence: Dr. Ayush Agarwal, Department of Neurology, Room 704, CN Center, All India Institute of Medical Sciences, New Delhi - 110 029, India.
E-mail: ayushthetaurian@gmail.com

Submitted: 10-Jul-2023 **Revised:** 10-Aug-2023 **Accepted:** 21-Aug-2023
Published: 25-Sep-2023

DOI: 10.4103/aian.aian_608_23