Massive and exclusive pontocerebellar damage in mitochondrial disease and *NUBPL* mutations

Figure Brain MRI (1.5 T) and ^{18}F FDG-PET

(A) Infratentorial level. MRS-H1-TE144, sagittal T1, axial T2 show lactate peaks with cerebellum and anterior pons anomalies (arrows). (B) Supratentorial level. MRS-H1-TE144, axial T2, coronal fluid-attenuated inversion recovery (FLAIR) show normal MRI. Note cerebellar atrophy on FLAIR. (C) Functional images (cerebellar axial arterial spin labeling, coronal ^{18}F FDG-PET) show increased blood flow and decreased glucose metabolism in the cerebellum and normal supratentorial images.

A 23-year-old man had progressive nystagmus, cerebellar ataxia, pyramidal signs, and slurred speech since toddlerhood. MRI showed T2 hyperintensity of the cerebellum, the anterior brainstem, and the pyramidal tract, sparing the pontine tegmentum (figure, A). Lack of cerebellar NAA and choline on proton magnetic resonance spectroscopy, glucose hypometabolism on ^{18}F FDG-PET, and elevated cerebellar lactate suggested mitochondrial disease.^{1,2} Increased cerebellar blood flow suggested vessel proliferation, consistent with mitochondrialopathy (figure, C). Skeletal muscle mitochondrial complex I activity was 31% of control. There was compound heterozygosity for 2 *NUBPL* mutations: c.205_206delGT, producing a premature stop codon (p.Val69Tyrfs*80); and c.815-217T>C, creating a splicing site and frameshift (p.Asp273Glnfs*32).

Estelle Valerie Tenisch, MD, Anne-Sophie Lebre, MD, PhD, David Grévent, MD, Pascale de Lonlay, MD, PhD, Marlene Rio, MD, PhD, Monica Zilbovicius, MD, PhD, Benoît Funalot, MD, PhD, Isabelle Desguerre, MD, PhD, Francis Brunelle, MD, Agnès Rötig, MD, PhD, Arnold Mummich, MD, PhD, Nathalie Boddaert, MD, PhD, Paris, France
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Correspondence & reprint requests to Dr. Tenisch: estelle.tenisch@gmail.com

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