Teaching NeuroImages: Hypomyelinating leukodystrophy with hypodontia due to *POLR3B*

Look into a leukodystrophy's mouth

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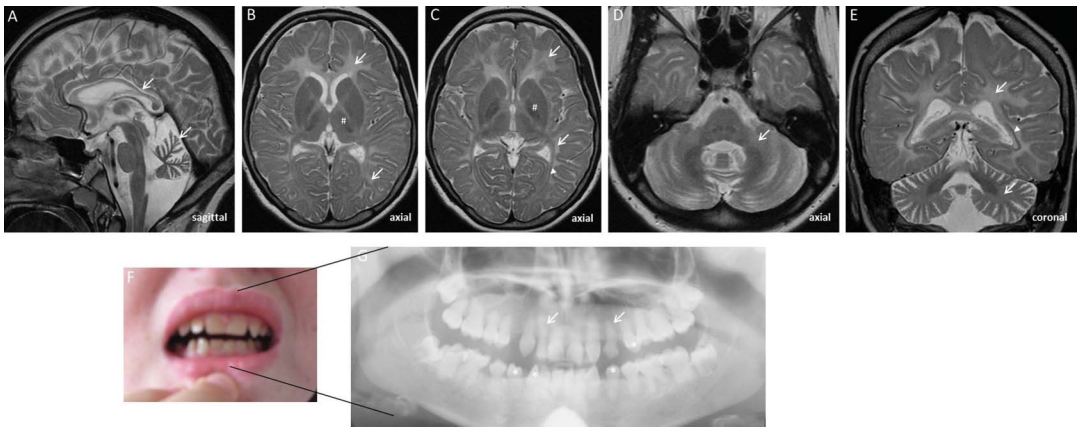
Figure T2-weighted MRI and dental X-ray



MRI shows diffuse hyperintense cerebral and cerebellar hypomyelination (B–E; arrows), relatively sparing the (hypointense) anterolateral thalami, globi pallidi (B, C; number sign), and optic radiations (C, E; arrowhead), as well as vermian cerebellar atrophy and thin corpus callosum (A; arrows). X-ray specifies teeth abnormalities (F), revealing persistent milk teeth (arrows) and hypoplastic crowns and roots (G; asterisks).

An 18-year-old German woman presented with progressive cerebellar ataxia since early childhood, delayed cognitive development, and hypogonadotropic hypogonadism. MRI demonstrated diffuse cerebral hypomyelination, cerebellar atrophy, and thin corpus callosum; x-ray revealed persistent milk teeth and hypoplastic crowns and roots (figure), indicative of 4H syndrome (hypomyelination, hypodontia, hypogonadotropic hypogonadism). *POLR3B* sequencing[1] revealed 2 compound heterozygous mutations (C527R [C.1579T>C] and the common ancestral V523E [C.1568T>A][2]).

These characteristic MRI and dental findings[1] help to identify Pol-III–associated leukodystrophies in the substantial share of patients with unexplained leukodystrophy and facilitate straightforward genetic diagnostics. *POLR3A* and *POLR3B* mutations are common in hypomyelinating leukodystrophies, even when hypogonadotropic hypogonadism or hypodontia is absent.[2]

AUTHOR CONTRIBUTIONS

Dr. Synofzik: acquisition of data, design and conceptualization of the study, revising the manuscript. Dr. Bernard: acquisition of data, revising the manuscript. Dr. Lindig: acquisition of data, revising the manuscript. Dr Gburek-Augustat: acquisition of data, revising the manuscript.

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