Hypomyelinating leukodystrophy with hypodontia due to POLR3B

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 revealed 2 compound heterozygous mutations (C527R [C.1579T>C] and the common ancestral V523E [C.1568T>A]).

These characteristic MRI and dental findings 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.

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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Matthias Synofzik, Geneviève Bernard, Tobias Lindig, et al.
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