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

Look into a leukodystrophy's mouth

Matthis Synofzik, MD
Geneviève Bernard, MD,
MSc, FRCPC
Tobias Lindig, MD
Janina Gburek-Augustat,
MD

Correspondence to
Dr Synofzik:
matthis.synofzik@uni-tuebingen.de

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* sequencing¹ revealed 2 compound heterozygous mutations (C527R [C.1579T>C] and the common ancestral V523E [C.1568T>A])².

These characteristic MRI and dental findings¹ 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.

STUDY FUNDING

No targeted funding reported.

DISCLOSURE

M. Synofzik received research grants by the Volkswagen Stiftung, the Robert Bosch Stiftung, and UK ataxia, and honoraria from Actelion Pharmaceuticals. G. Bernard has received honoraria from Santhera Pharmaceuticals and Actelion Pharmaceuticals. T. Lindig and J. Gburek-Augustat report no disclosures. Go to Neurology.org for full disclosures.

REFERENCES

1. Tetreault M, Choquet K, Orcesi S, et al. Recessive mutations in *POLR3B*, encoding the second largest subunit of Pol III, cause a rare hypomyelinating leukodystrophy. *Am J Hum Genet* 2011;89:652–655.
2. Daoud H, Tetreault M, Gibson W, et al. Mutations in *POLR3A* and *POLR3B* are a major cause of hypomyelinating leukodystrophies with or without dental abnormalities and/or hypogonadotropic hypogonadism. *J Med Genet* 2013;50:194–197.

Download teaching slides:
www.neurology.org

From the Department of Neurodegenerative Diseases, Hertie-Institute for Clinical Brain Research (M.S.), German Research Center for Neurodegenerative Diseases (DZNE) (M.S.), and Department of Neuroradiology (T.L.), University of Tübingen, Germany; Departments of Pediatrics, Neurology, and Neurosurgery (G.B.), Montreal Children's Hospital, McGill University Health Center, Canada; and the Department of Pediatric and Developmental Neurology (J.G.-A.), University Children's Hospital, Tübingen, Germany.

Neurology[®]

Teaching *NeuroImages*: Hypomyelinating leukodystrophy with hypodontia due to *POLR3B*: Look into a leukodystrophy's mouth

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

Neurology 2013;81:e145

DOI 10.1212/01.wnl.0000435300.64776.7e

This information is current as of November 4, 2013

Updated Information & Services	including high resolution figures, can be found at: http://n.neurology.org/content/81/19/e145.full
Supplementary Material	Supplementary material can be found at: http://n.neurology.org/content/suppl/2013/11/02/81.19.e145.DC1
References	This article cites 2 articles, 1 of which you can access for free at: http://n.neurology.org/content/81/19/e145.full#ref-list-1
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): All Genetics http://n.neurology.org/cgi/collection/all_genetics All Pediatric http://n.neurology.org/cgi/collection/all_pediatric Developmental disorders http://n.neurology.org/cgi/collection/developmental_disorders Leukodystrophies http://n.neurology.org/cgi/collection/leukodystrophies Spinocerebellar ataxia http://n.neurology.org/cgi/collection/spinocerebellar_ataxia
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.neurology.org/about/about_the_journal#permissions
Reprints	Information about ordering reprints can be found online: http://n.neurology.org/subscribers/advertise

Neurology® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2013 American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.