

Complete Agenesis of Corpus Callosum in *KCNQ2*-Related Neonatal Epileptic Encephalopathy

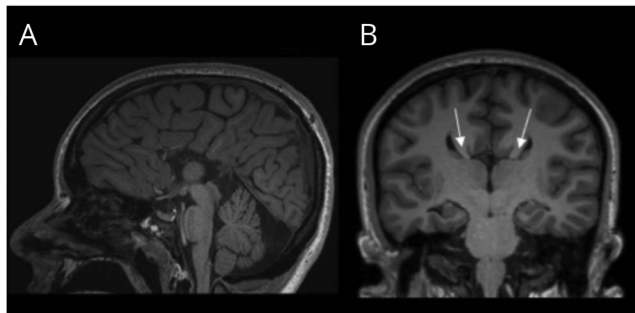
Laura Licchetta, MD, PhD,* Raffaella Minardi, PhD,* Lorenzo Muccioli, MD, Laura Ludovica Gramegna, MD, David Neil Manners, PhD, Caterina Tonon, MD, PhD, Francesca Bisulli, MD, PhD, and Paolo Tinuper, MD

Correspondence

Dr. Licchetta
laura.licchetta@austl.bo.it

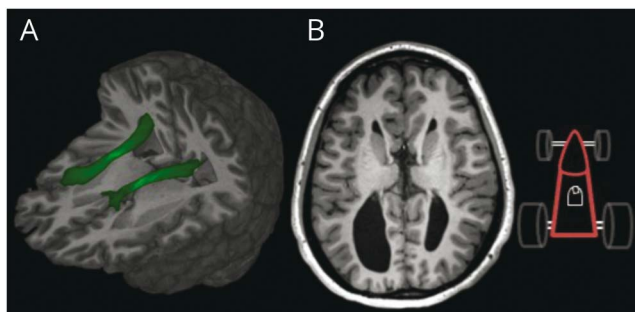
Neurol Genet 2022;8:e200042. doi:10.1212/NXG.000000000200042

Figure 1 Complete Agenesis of Corpus Callosum and Probst Bundles



(A) Sagittal T1-weighted image: complete agenesis of corpus callosum. (B) Coronal T1-weighted image: Probst bundles (arrows) (i.e., aberrant collections of axons that would normally form the corpus callosum but fail to cross the midline); hippocampal malrotation.

Figure 2 Tractography and Racing-Car Sign



(A) 3D-DTI tractography reconstruction: Probst bundles running parallel to the interhemispheric fissure with anteroposterior orientation. (B) Axial T1-weighted image: asymmetric "racing-car sign." DTI = diffusion tensor imaging.

This 22-year-old female patient presented with tonic seizures on the second day of life. Psychomotor delay and intellectual disability then became evident. Seizures were initially controlled by phenobarbital, except for rare relapses. The patient experienced 1–2 seizures/yr between ages 12 and 20 years; since then, she has been seizure-free on oxcarbazepine and valproate.

She also had partial growth hormone deficiency.

EEG showed posterior epileptiform abnormalities. 3T-brain MRI disclosed complete agenesis of corpus callosum (ACC) (Figures 1 and 2).

*These authors contributed equally to this work.

From the IRCCS Istituto Delle Scienze Neurologiche di Bologna (L.L., R.M., F.B., P.T.), Full Member of European Reference Network EpicARE; Department of Biomedical and Neuromotor Sciences (L.M., L.L.G., D.N.M., C.T., F.B., P.T.), University of Bologna; and Functional and Molecular Neuroimaging Unit (L.L.G., C.T.), IRCCS Istituto Delle Scienze Neurologiche di Bologna, Italy.

Go to [Neurology.org/NG](https://www.neurology.org/NG) for full disclosures. Funding information is provided at the end of the article.

The Article Processing Charge was funded by the authors.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0 (CC BY-NC-ND), which permits downloading and sharing the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Karyotype and Array - Comparative Genomic Hybridization were normal. An in silico ACC multigene panel extracted from whole exome sequencing (WES; mean coverage: $\times 52$; read length: 150 bp) in 2021 was negative.

WES analysis showed a heterozygous missense variant in *KCNQ2* (NM_172107.4), p.Arg353Cys, arising de novo. The ACMG guidelines¹ classify the variant as pathogenic (PM1, PM5, PM2, PP2, PP3, PPS, PS1, PS2).

The patient was diagnosed with *KCNQ2*-related neonatal epileptic encephalopathy.

KCNQ2-associated brain abnormalities include thinning of the corpus callosum² but complete ACC has never been reported.

Acknowledgment

The authors thank the patient and her family for participating. Thanks to the Epi25 consortium, supported by National Human Genome Research Institute Grant UM1 HG008895.

Study Funding

The authors report no targeted funding.

Disclosure

The authors report no disclosures relevant to the manuscript. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/NG.

Publication History

Received by *Neurology: Genetics* June 29, 2022. Accepted in final form September 22, 2022. Submitted and externally peer reviewed. The handling editor was Stefan M. Pulst, MD, Dr med, FAAN.

Appendix Authors

Name	Location	Contribution
Laura Licchetta, MD, PhD	IRCSS Istituto delle Scienze Neurologiche di Bologna, Full Member of European Reference Network EpiCARE, Bologna, Italy	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data

Appendix (continued)

Name	Location	Contribution
Raffaella Minardi, PhD	IRCSS Istituto delle Scienze Neurologiche di Bologna, Full Member of European Reference Network EpiCARE, Bologna, Italy	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data
Lorenzo Muccioli, MD	Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy	Major role in the acquisition of data
Laura Ludovica Gramegna, MD	Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy; Functional and Molecular Neuroimaging Unit, IRCCS Istituto delle Scienze neurologiche di Bologna, Italy	Major role in the acquisition of data; analysis or interpretation of data
David Neil Manners, PhD	Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy	Major role in the acquisition of data; analysis or interpretation of data
Caterina Tonon, MD, PhD	Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy; Functional and Molecular Neuroimaging Unit, IRCCS Istituto delle Scienze neurologiche di Bologna, Bologna, Italy	Analysis or interpretation of data
Francesca Bisulli, MD, PhD	IRCSS Istituto delle Scienze Neurologiche di Bologna, Full Member of European Reference Network EpiCARE, Bologna, Italy; Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy	Drafting/revision of the manuscript for content, including medical writing for content
Paolo Tinuper, MD	IRCSS Istituto delle Scienze Neurologiche di Bologna, Full Member of European Reference Network EpiCARE, Bologna, Italy; Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy	Study concept or design

References

- Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med*. 2015;17(5):405-424. doi: 10.1038/gim.2015.30.
- Weckhuysen S, Ivanovic V, Hendrickx R, et al. Extending the *KCNQ2* encephalopathy spectrum: clinical and neuroimaging findings in 17 patients. *Neurology*. 2013; 81(19):1697-1703. doi: 10.1212/01.wnl.0000435296.72400.a1.

Neurology[®] Genetics

Complete Agenesis of Corpus Callosum in *KCNQ2*-Related Neonatal Epileptic Encephalopathy

Laura Licchetta, Raffaella Minardi, Lorenzo Muccioli, et al.

Neurol Genet 2022;8;

DOI 10.1212/NXG.0000000000200042

This information is current as of November 7, 2022

Updated Information & Services	including high resolution figures, can be found at: http://ng.neurology.org/content/8/6/e200042.full.html
References	This article cites 2 articles, 0 of which you can access for free at: http://ng.neurology.org/content/8/6/e200042.full.html##ref-list-1
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): All Epilepsy/Seizures http://ng.neurology.org/cgi/collection/all_epilepsy_seizures All Genetics http://ng.neurology.org/cgi/collection/all_genetics MRI http://ng.neurology.org/cgi/collection/mri
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://ng.neurology.org/misc/about.xhtml#permissions
Reprints	Information about ordering reprints can be found online: http://ng.neurology.org/misc/addir.xhtml#reprintsus

Neurol Genet is an official journal of the American Academy of Neurology. Published since April 2015, it is an open-access, online-only, continuous publication journal. Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Academy of Neurology. All rights reserved. Online ISSN: 2376-7839.

