

Teaching NeuroImage: Human Polymerase Gamma Gene (*POLG*) Disorder Presenting as Refractory Status Epilepticus

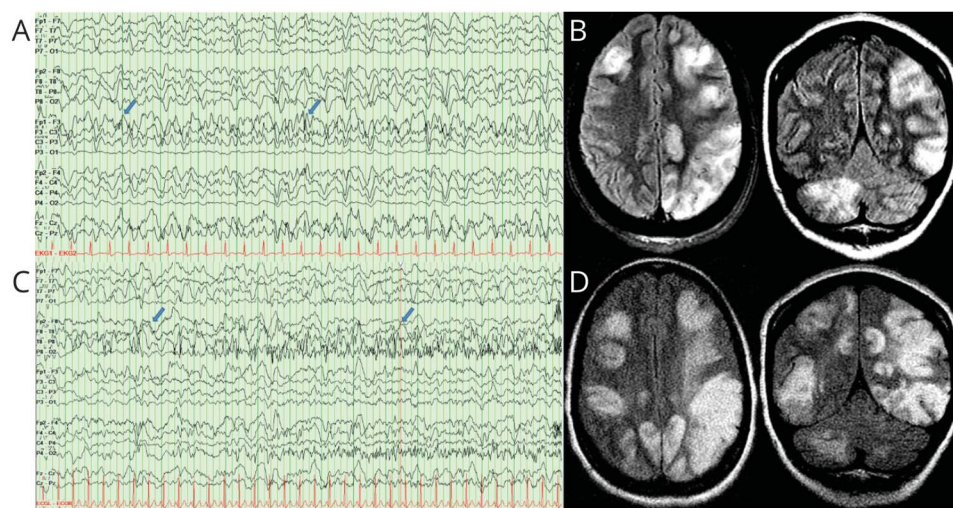
Hernan Nicolas Lemus, MD, Dewitt Pyburn, MD, Clover Youn, DO, John Liang, MD, Arash Yousefi, MD, Rachel Saunders-Pullman, MD, MPH, Gabriela Tantillo, MD, Lara Marcuse, MD, and Madeline Fields, MD

Neurology® 2021;97:e747-e748. doi:10.1212/WNL.00000000000012105

Correspondence

Dr. Lemus
Hernannicolas.
lemusesquivel@mountsinai.org

Figure 1 EEG and MRI of Index Patient



(A) EEG on day of admission shows a longitudinal bipolar montage with left frontocentral focal status epilepticus (blue arrows). (B) Fluid-attenuated inversion recovery (FLAIR) MRI shows multifocal hyperintensities. (C) EEG later in the hospital course shows right temporo-occipital region seizures (blue arrows). (D) FLAIR MRI shows worsening of the hyperintensities with involvement of the right hemisphere.

A 31-year-old woman with severe childhood-onset dysmotility syndrome was admitted for encephalopathy and seizures. Video EEG demonstrated electrographic seizures of multifocal onset refractory to multiple antiseizure medications (figure 1, A and C). MRI of the brain revealed multiple hyperintensities (figure 1B) that progressed (figure 1D). Infectious, immunologic, and neoplastic workup was unremarkable. A comprehensive epilepsy panel demonstrated a human polymerase gamma gene (*POLG*) likely pathogenic variant, c.3401 (c.3401A>G), previously reported as recessive, and a novel variant of unknown significance, c.2725 (c.2725 G>A). We hypothesize both variants are predicted to act in a compound heterozygous fashion. *POLG* disorders present with a discrete phenotype in adults; diagnosis is critical as valproate can precipitate liver failure^{1,2} (figure 2).

Acknowledgment

The authors thank George A. Diaz, MD, PhD, for genetic advice on the patient.

MORE ONLINE

Teaching slides

links.lww.com/WNL/B394

From the Department of Neurology (H.N.L., D.P., C.Y., A.Y., R.S.-P.), Icahn School of Medicine at Mount Sinai Downtown; Department of Neurology and Neurosurgery (J.L.), Icahn School of Medicine at Mount Sinai West; and Department of Neurology (G.T., L.M., M.F.), Icahn School of Medicine at Mount Sinai Hospital, New York, NY.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Figure 2 Clinical Spectrum of *POLG*-Related Disorders

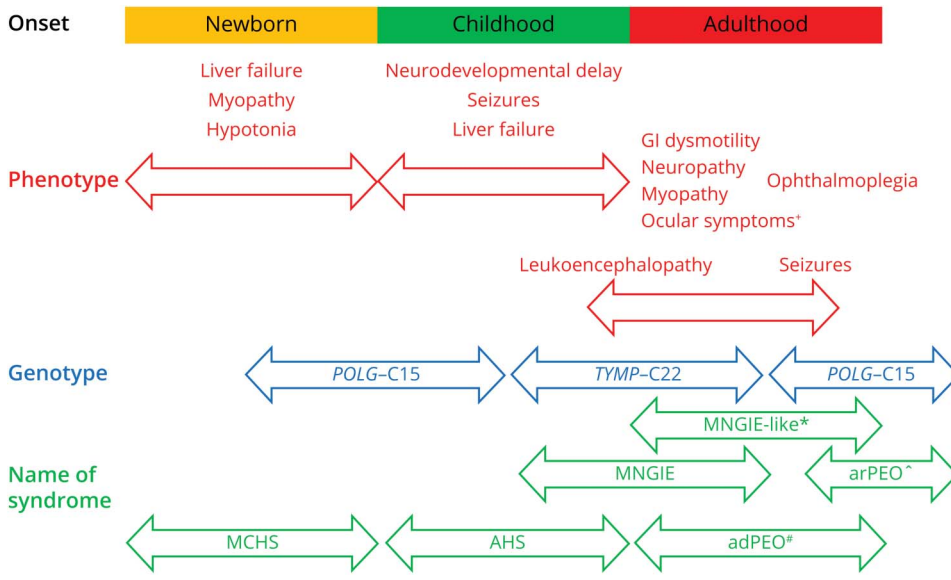


Figure 2 is based on references 1 and 2. adPEO = autosomal dominant progressive external ophthalmoplegia; AHS = Alpers-Huttenlocher syndrome; arPEO = autosomal recessive progressive external ophthalmoplegia; C = chromosome; GI = gastrointestinal; MCHS = myocerebrohepatopathy; MNGIE = mitochondrial neurogastrointestinal encephalopathy; *POLG* = human polymerase gamma gene; *TYMP* = thymidine phosphorylase gene. *Same phenotype as mitochondrial neurogastrointestinal encephalopathy but without leukoencephalopathy. +Ptosis and ophthalmoplegia without systemic symptoms. #Also ataxia, depression, parkinsonism, hypogonadism, and cataracts.

Study Funding

No targeted funding reported.

Disclosure

Dr. Lemus, Dr. Pyburn, Dr. Youn, Dr. Liang, and Dr. Yousefi report no disclosures relevant to the manuscript. Dr. Saunders-Pullman reports support from NIH U01-NS107016-01A1, Empire Clinical Research Investigator Program, the Bigglesworth Family Foundation, and Bachmann-Strauss Professorship. Dr. Tantillo previously held shares in a diversified index health care exchange traded fund unrelated to this study (2019). Dr. Marcuse and Dr. Fields report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

Appendix Authors

| Name | Location | Contribution |
|-----------------------------|--|--|
| H. Nicolas Lemus, MD | Icahn School of Medicine at Mount Sinai Downtown | Designed and conceptualized study, drafted the manuscript for intellectual content |
| Dewitt Pyburn, MD | Icahn School of Medicine at Mount Sinai Downtown | Designed and conceptualized study, drafted the manuscript for intellectual content |
| Clover Youn, DO | Icahn School of Medicine at Mount Sinai Downtown | Drafted the manuscript for intellectual content |

Appendix (continued)

| Name | Location | Contribution |
|---|--|-----------------------------------|
| John Liang, MD | Icahn School of Medicine at Mount Sinai West | Critical review of the manuscript |
| Arash Yousefi, MD | Icahn School of Medicine at Mount Sinai Downtown | Critical review of the manuscript |
| Rachel Saunders-Pullman, MD, MPH | Icahn School of Medicine at Mount Sinai Downtown | Critical review of the manuscript |
| Gabriela Tantillo, MD | Icahn School of Medicine at Mount Sinai Hospital | Critical review of the manuscript |
| Lara Marcuse, MD | Icahn School of Medicine at Mount Sinai Hospital | Critical review of the manuscript |
| Madeline Fields, MD | Icahn School of Medicine at Mount Sinai Hospital | Critical review of the manuscript |

References

1. Rahman S, Copeland WC. *POLG*-related disorders and their neurological manifestations. *Nat Rev Neurol*. 2019;15(1):40-52.
2. Hikmat O, Tzoulis C, Chong WK, et al. The clinical spectrum and natural history of early-onset diseases due to DNA polymerase gamma mutations. *Genet Med*. 2017; 19(11):1217-1225.

Neurology®

Teaching NeuroImage: Human Polymerase Gamma Gene (*POLG*) Disorder Presenting as Refractory Status Epilepticus

Hernan Nicolas Lemus, Dewitt Pyburn, Clover Youn, et al.
Neurology 2021;97:e747-e748 Published Online before print April 30, 2021
DOI 10.1212/WNL.00000000000012105

This information is current as of April 30, 2021

| | |
|---|---|
| Updated Information & Services | including high resolution figures, can be found at: http://n.neurology.org/content/97/7/e747.full |
| References | This article cites 2 articles, 0 of which you can access for free at: http://n.neurology.org/content/97/7/e747.full#ref-list-1 |
| Subspecialty Collections | This article, along with others on similar topics, appears in the following collection(s): EEG http://n.neurology.org/cgi/collection/eeg_ EEG; see Epilepsy/Seizures http://n.neurology.org/cgi/collection/eeg_see_epilepsy-seizures Gastrointestinal http://n.neurology.org/cgi/collection/gastrointestinal Status epilepticus http://n.neurology.org/cgi/collection/status_epilepticus |
| 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 © 2021 American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.

