

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

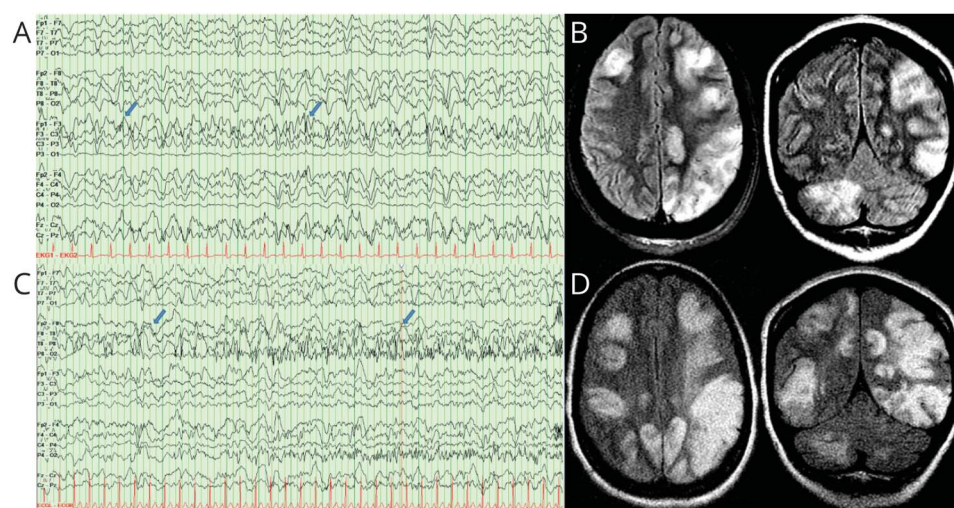
Hernan Nicolas Lemus, MD, Dewitt Pyburn, MD, Clover Youn, DO, John Liang, MD, Arash Yousefi, MD, Rachel Saunders-Pullman, MD, MPH, Gabriela Tantillo, MD, Lara Marcuse, MD, and Madeline Fields, MD

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**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 dysmaturity 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<sup>1,2</sup> (figure 2).

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**Figure 2** Clinical Spectrum of *POLG*-Related Disorders

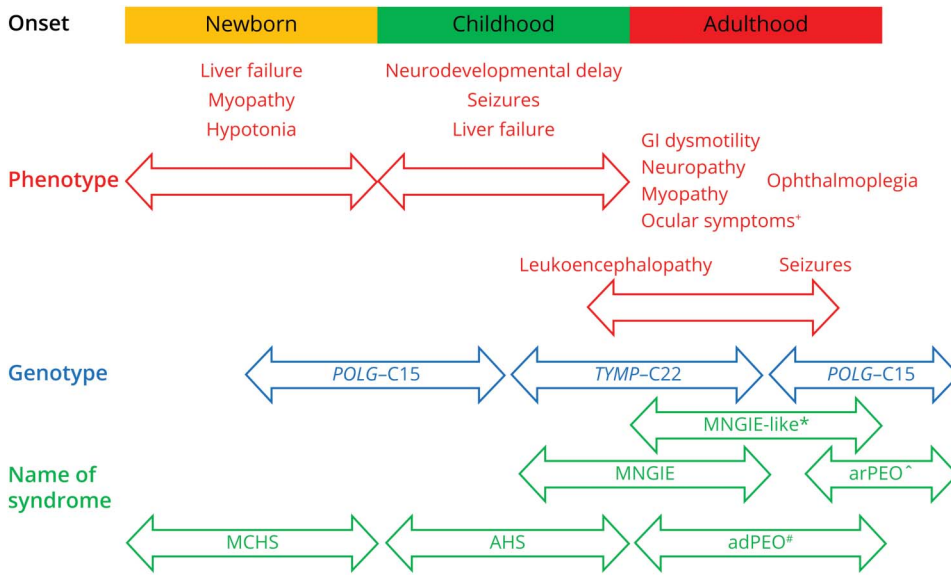


Figure 2 is based on references 1 and 2. adPEO = autosomal dominant progressive external ophthalmoplegia; AHS = Alpers-Huttenlocher syndrome; arPEO = autosomal recessive progressive external ophthalmoplegia; C = chromosome; GI = gastrointestinal; MCHS = myocerebrohepatopathy; MNGIE = mitochondrial neurogastrointestinal 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.

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**Appendix** Authors

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

**Appendix** (continued)

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

**References**

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