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

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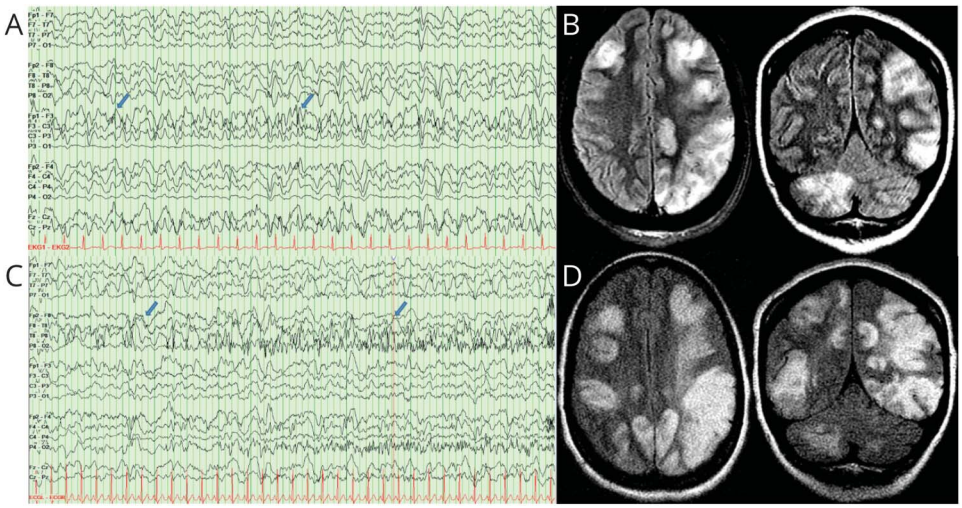
Figure 1 EEG and MRI of Index Patient



(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 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).

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

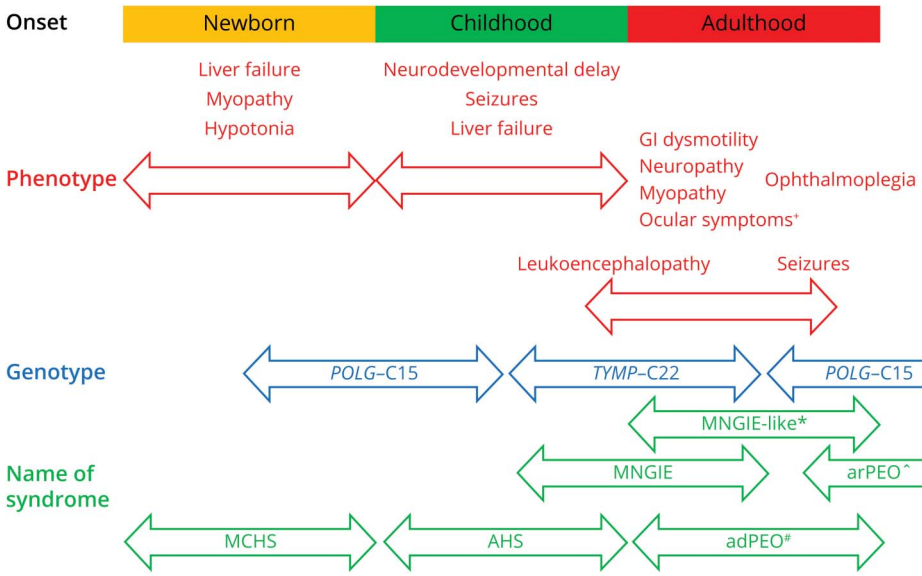

Figure 2 is based on references 1 and 2. adPEO = autosomal dominant progressive external ophthalmoplegia; AHS = Alpers-Huttenlocher syndrome; arPEO = autosomal recessive progressive external ophthalmoplegia; C = chromosome; GI = gastrointestinal; MCHS = myocerebrohepatopathy; MNGIE = mitochondrial neurogastrointestinal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

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Disclosure

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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
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John Liang, MD	Icahn School of Medicine at Mount Sinai West	Critical review of the manuscript
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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

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