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

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

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Teaching Slides - [http://links.lww.com/WNL/B394](http://links.lww.com/WNL/B394)
References:


Figure 1. EEG and MRI of index patient. A. EEG on day of admission showing a longitudinal bipolar montage with left frontocentral focal status epilepticus (blue arrows). B. FLAIR MRI showing multifocal hyperintensities. C. EEG later in the hospital course showing right temporo-occipital region seizures (blue arrows). D. FLAIR MRI showing worsening of the hyperintensities with involvement of the right hemisphere.
Figure 2. Clinical spectrum of POLG related disorders. Figure based on references ¹ and ².

POLG, human polymerase gamma gene. TYMP, thymidine phosphorylase gene. C, chromosome. MCHS, myocerebrohepatopathy. AHS, Alpers-Huttenlocher syndrome. MNGIE, mitochondrial neurogastrointestinal encephalopathy. arPEO, autosomal recessive progressive external ophthalmoplegia. adPEO, autosomal dominant progressive external ophthalmoplegia. +, ptosis and ophthalmoplegia. *, same phenotype as MGNIE but without leukoencephalopathy. ^, ptosis and ophthalmoplegia without systemic symptoms. #, also ataxia, depression, parkinsonism, hypogonadism and cataracts.
Onset

- **Newborn**
  - Liver failure
  - Myopathy
  - Hypotonia

- **Childhood**
  - Neurodevelopmental delay
  - Seizures

- **Adulthood**
  - GI dysmotility
  - Neuropathy
  - Myopathy
  - Ophthalmoplegia
  - Ocular symptoms

Phenotype

- Leukoencephalopathy
- Seizures

Genotype

- **POLG-C15**
- **TYMP-C22**
- **POLG-C15**

Name of syndrome

- **MCHS**
- **AHS**
- **adPEO**
- **arPEO**
- **MNGIE**
- **MNGIE-like**
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