Focal epileptogenic lesion in a patient with epileptic encephalopathy secondary to SRCAP gene. Double pathology or linked disorders?

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BACKGROUND

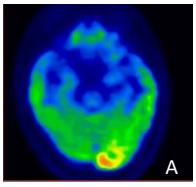
Epileptic encephalopathies with structural and genetic causes are challenging to diagnose and treat. We report **a 24-year-old male with drug-resistant epilepsy**, hippocampal sclerosis, and a **de novo SRCAP mutation**, highlighting potential genotype–phenotype correlations.

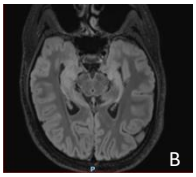
MATERIALS AND METHODS:

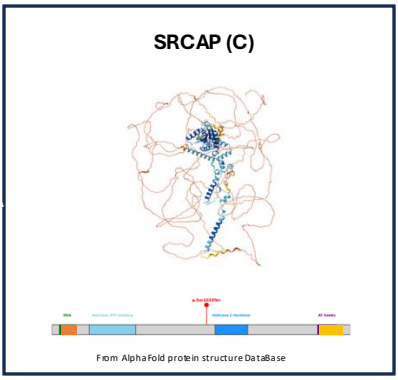
The patient's evaluation included: clinical history, neuropsychological assessment, neurological examination, 24-hour video-EEG monitoring, brain MRI and PET, array-CGH, and in trio-WES

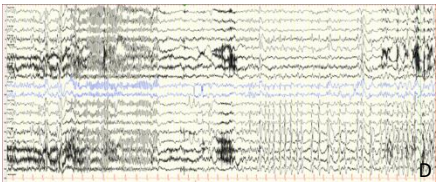
CASE REPORT

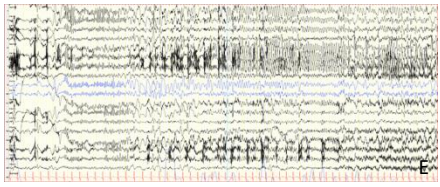
History	Epilepsy began at 11 years with focal seizures, later evolving into bilateral tonic–clonic convulsion and status epilepticus. He currently experiences monthly drug-resistant focal impaired awareness seizures.
Neuropsychology	**Intellectual disability (IQ 44)** and learning difficulties.
Clinical picture	Dysprosody and craniofacial dysmorphisms
Imaging	Initial MRI showed left hippocampal swelling. Current MRI and PET demonstrated **left hippocampal sclerosis** (figure A,B)**.**
EEG	Interictal EEG showed frequent**, diffuse fronto-temporal spike-and-wave discharges without a clear hemispheric predominance**. During **three recorded seizures,** EEG showed discharges **with variable lateralization** that rapidly spread (figure D,E) .
Genetics (WES – array-CGH)	De novo **truncating SRCAP mutation (c.4976C>G, p.Ser1659Ter) in exon 25**, potentially explaining both neurodevelopmental and epileptic features [1,2] (figure C).











DISCUSSION & CONCLUSION:

SRCAP is crucial for early neural circuit formation. **Chromatin remodeling gene mutations may disrupt cortical and subcortical network maturation, explaining coexisting structural abnormalities and widespread seizures**. Hippocampal sclerosis may also arise secondary to prolonged seizures (e.g., SCN1A). This case may highlight the dual role of chromatin remodeling genes in neurodevelopmental disorders and epilepsy, emphasizing the importance of epigenetic regulators in epileptogenesis.

Bibliography:

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