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P33. A CASE OF DEVELOPMENTAL ENCEPHALOPATHY CAUSED BY A DE NOVO KCNB1 GENE MUTATION

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Background: De novo KCNB1 mutations have been identified in patients with early onset epileptic encephalopathies (EE) ranging from West to Lennox-Gastaut syndrome. KCNB1 gene encodes the Kv2.1 voltage-gated potassium channels, critical for membrane repolarization during repetitive stimulation. Here we describe a 17-month-old girl with global developmental delay, post-natal microcephaly and pharmaco-resistant epilepsy caused by de novo mutation in KCNB1.
Case description: the patient is the first daughter of healthy non-consanguineous parents. At 9months of life, clinical examination revealed an axial hypotonia and she presented daily episodes of motor arrest followed by spasms in flexion, occurring especially upon awakening. Electroencephalogram (EEG) revealed normal background activity with focal (left temporal) or rare multifocal spikes, without a pattern of hypsarrhythmia. She was immediately treated with ACTH, but spasms relapsed at the end of therapy. Seizures were resistant to valproic acid and levetiracetam. A therapy with topiramate reached a partial control of seizures. Brain magnetic resonance, fundus oculi, auditory and visual evoked potentials, metabolic screening, CGH-array were all normal. Next generation sequencing panel for EE revealed a novel de novo mutation (c.1045G>7-p.Val349Phe) in the S5 domain of the KCNB1 gene. At her last evaluation at 16 months, she did not reach the upright position, persisting a truncal hypotonia, she had a poor eye contact and reduced response to social interactions. A post-natal microcephaly was also evident.
Conclusion: This case expands the phenotypic spectrum of epilepsies associated with KCNB1 variants. Functional characterization of mutant channels will be crucial for target therapy.