Acute encephalopathy after head trauma in a patient with a RHOBTB2 mutation

**Objective** De novo missense mutations in the RHOBTB2 gene have been described as causative for developmental and epileptic encephalopathy.

**Methods** The clinical phenotype of this disorder includes early-onset epilepsy, severe intellectual disability, postnatal microcephaly, and movement disorder. Three RHOBTB2 patients have been described with acute encephalopathy and febrile epileptic status. All showed severe EEG abnormalities during this episode and abnormal MRI with hemisphere swelling or reduced diffusion in various brain regions.

**Results** We describe the episode of acute encephalopathy after head trauma in a 5-year-old RHOBTB2 patient. At admission, Glasgow coma scale score was E4M4V1. EEG was severely abnormal showing a noncontinuous pattern with slow activity without epileptic activity indicating severe encephalopathy. A second EEG on day 8 was still severely slowed and showed focal delta activity frontotemporal in both hemispheres. Gradually, he recovered, and on day 11, he had regained his normal reactivity, behavior, and mood. Two months after discharge, EEG showed further decrease in slow activity and increase in normal electroencephalographic activity. After discharge, parents noted that he showed more hyperkinetic movements compared to before this period of encephalopathy. Follow-up MRI showed an increment of hippocampal atrophy. In addition, we summarize the clinical characteristics of a second RHOBTB2 patient with increase of focal periventricular atrophy and development of hemiparesis after epileptic status.

**Conclusion** Acute encephalopathy in RHOBTB2 patients can also be triggered by head trauma.

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**TGM6 L517W is not a pathogenic variant for spinocerebellar ataxia type 35**

**Objective** To investigate the pathogenicity of the TGM6 variant for spinocerebellar ataxia 35 (SCA35), which was previously reported to be caused by pathogenic mutations in the gene TGM6.

**Methods** Neurologic assessment and brain MRI were performed to provide detailed description of the phenotype. Whole-exome sequencing and dynamic mutation analysis were performed to identify the genotype.

**Results** The proband, presenting with myoclonic epilepsy, cognitive decline, and ataxia, harbored both the TGM6 p.L517W variant and expanded CAG repeats in gene ATN1. Further analysis of the other living family members in this pedigree revealed that the CAG repeat number was expanded in all the patients and within normal range in all the unaffected family members. However, the TGM6 p.L517W variant was absent in 2 affected family members, but present in 3 healthy individuals.

**Conclusion** The nonsegregation of the TGM6 variant with phenotype does not support this variant as the disease-causing gene in this pedigree, questioning the pathogenicity of TGM6 in SCA35.

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