STXBP1 as a Novel Gene for Sleep-Related Hypermotor Epilepsy: A Video-EEG Documented Case Report

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Objectives

Sleep-related hypermotor epilepsy (SHE) is a rare syndrome that presents with hyperkinetic asymmetric tonic/dystonic seizures, mainly during sleep. Certainty of diagnosis can be categorized into 3 levels: witnessed (possible) SHE, video documented (clinical) SHE, and video-EEG documented (confirmed) SHE. The role of various genes (CHRNA4, CHRNB2, CHRNA2, KCNT1, DEPDC5, NPRL2, NPRL3, and PRIMA1) has previously been reported. The STXBP1 gene is phenotypically associated with early infancy epileptic encephalopathy 4. It's also been linked to Ohtahara Syndrome, West Syndrome, and Dravet Syndrome.

In this case report, we present a patient who was clinically assumed to have nocturnal frontal lobe epilepsy and was diagnosed with video-EEG documented SHE, but who had a STXBP1 mutation and did not fit the clinical phenomenology of the STXBP1 mutations.

Case Report

A nine-year-old girl was admitted to our Video-EEG unit for seizure and sleep disorder differentiation. Her medical history revealed that she experienced rapid and aimless movements, particularly in her extremities, after waking up unexpectedly in the middle of the night and rising in bed. Her seizures began at the age of five. She has had an increase in the number of seizures over the previous two months while on antiepileptic medication. Almost all of her seizures occurred during sleep. In her video EEG recordings, it was observed that the background rhythm was appropriate for her age. During the event, ictal activity starting from the left frontotemporal region was observed in the EEG. Her seizures were classified as focal onset, impaired of awereness, motor, hyperkinetic seizures. Genetic analysis was requested from the patient. As a result, a heterozygous mutation was detected in the STXBP1 gene (c.847G>A (p.283K) (p.Glu283Lys)). This gene mutation, which is associated with Dravet Syndrome, was detected for the first time in a case of Video-EEG documented SHE.

Discussion

In a majority of SHE patients, the etiology is unknown. Genetic causes are one of the identified etiologies. The presented case extends the list of SHE-related genes to include STXBP1. The conventional phenotypic features caused by this gene mutation were severe than our patient's clinical findings. Future functional studies may reveal genotype-phenotype concordance.

Acknowledge : We would like to express our gratitude to our patient and his family for cooperating with us in this study. We are also grateful to all colleagues taking part in this study.

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