A Rare Cause of Developmental Epileptic Encephalopathy; UBA5 Gene Mutation

Merve Hilal Dolu, Pakize Cennetoğlu, İhsan Kafadar

Basaksehir Cam and Sakura City Hospital

ICNC 2022
17th INTERNATIONAL CHILD NEUROLOGY CONGRESS
ANTALYA, TURKEY | OCTOBER 3-7, 2022

ABSTRACT

Developmental epileptic encephalopathy-44 is an autosomal recessive neurologic disorder characterized by the early onset of refractory seizures. We describe a patient who had severe global developmental delay and early onset treatment resistant epilepsy with UBA5 gene mutation. Two months old female patient who had onset of seizures on day of life. She had severe developmental delay, axial hypotonia. Seizures were characterized by jeneralize tonic and myoclonic seizures with eye deviation. Electroencephalogram showed multifocal epileptiform discharges. Magnetic resonance imaging findings were diffuse cerebral and cerebellar atrophy with enlarged ventricles and thin corpus callosum. The metabolic workup was found normal. Despite the multiple antiepileptic drugs seizures couldn't stop. We identified an homozygous variant c.440A>G (p.His147Arg) in the UBA5 gene, a gene previously implicated in early infantile epileptic encephalopath-44. In addition, heterozygous variants were detected in the same gene in her parents. UBA5-related Early Epileptic Encephalopathy should be considered as an opinion in the diagnosis of patients with early onset treatment-resistant epilepsy and severe global developmental delay.

INTRODUCTION

Developmental epileptic encephalopathy-44 (DEE44) is an autosomal recessive neurologic disorder characterized by the early onset of refractory seizures usually in the first weeks or months of life, up to about 12 months of age. Here we describe a patient who had severe global developmental delay and early-onset treatment-resistant epilepsy with UBA5 gene mutation.

CASE

Two months old female patient who was born from consanguineous parents after normal pregnancy and delivery. She had severe global developmental delay, axial hypotonia and not-ability to track object. Head circumference was normal. We learned she had onset of seizures on day of life but before admitted our clinic she had no treatment at all. Seizures characterized by jeneralize tonic and myoclonic seizures with eye deviation. EEG showed multifocal epileptiform discharges predominant in occipital regions. Brain magnetic resonance imaging (MRI) findings were diffuse cerebral and cerebellar atrophy with enlarged ventricles and thin corpus callosum. The metabolic workup included arterial blood gas; serum and cerebro spinale fluıd (CSF) glucose, serum lactate, uric acid, ammonnia, creatine phosphokinase urinary ketone bodies, urine and CSF amino-acids, acylcarnitine profile and chromatography of organic acids in urine. But all of them found in normal ranges. We identified an homozygous variant c.440A>G (p.His147Arg) in the UBA5 gene, a gene previously implicated in early infantile epileptic encephalopath-44.

In addition, heterozygous variants were detected in the same gene in her parents. Despite the multiple antiepileptic drugs (phenobarbital, clobazam, clonazepam, levetiracetam, carbamazepine, topiramate, vigabatrin, midazolam and thiopental infusion) the patient continued to have multiple seizures per day.

CONCLUSIONS

UBA5-related Early Epileptic Encephalopathy should be considered as an opinion in the diagnosis of patients with early onset treatment-resistant epilepsy and severe global developmental delay.

REFERENCES

1. Muona M, Ishimura R. Biallelic Variants in UBA5 Link Dysfunctional UFM1 Ubiquitin-like Modifier Pathway to Severe Infantile-Onset Encephalopathy. The American Journal of Human Genetics 99, 1–12, September 1, 2016.
2. Mignon-Ravix C, Milh . Abnormal function of the UBA5 protein in a case of early developmental and epileptic encephalopathy with suppression-burst. Hum Mutat. 2018 Jul;39(7):934-938.
3. Colin E, Daniel J. Biallelic Variants in UBA5 Reveal that Disruption of the UFM1 Cascade Can Result in Early-Onset Encephalopathy. The American Journal of Human Genetics 99, 1–9, September 1, 2016