TBC1D24 gene Mutations Presented with Familial Infantile Myoclonic Epilepsy

Nefise Arıbaş ÖZ[1], Nesrin Ceylan[1], Abdüllatif Bakır[2], Hamit Özyürek[1]

1 Ankara City Hospital, Children's Hospital, Department of Pediatric Neurology 2 Dr. Sami Ulus Maternity and Children's Education and Research Hospital, Department of Medical Genetics

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

Introduction: TBC1D24 gene mutations are the cause of multiple rare disorders consists of varying degrees of intellectual disability, non-syndromic deafness, cortical malformations, and/or wide spectrum of epilepsies. Early-onset myoclonic epilepsy and drug resistant myoclonic seizures are the most common epilepsy phenotypes in TBC1D24 mutation. Interictal EEG and neuroimaging results are variable. There was no significant intrafamilial phenotypic variability in siblings having same mutations. Here we present two siblings with familial infantile myoclonic epilepsy associated TBC1D24 gene mutation.

Case 1: The older sister, aged of 36 months, was firstly admitted to the pediatric neurology outpatient clinic when she was 4 months old because of myoclonic jerks started in her lower extremities and then extending to her right arm and face. Additionally, hospitalization was occasional required due to prolonged generalized myoclonus or myoclonic status refractory to valproate, lamotrigine, clobazam, and clonazepam. Prenatal and natal history were uneventful. There was a first degree consanguinity between parent. Developmental milestones were normal at the beginning. Unfortunately, serious regression was observed over time.

Her head circumference was 45 cm (< 3rd p) microcephalic, other body measurements were compatible with her age (25-50th percentile). There is no dysmorphic finding. On neurological examination, she was conscious and her cranial nerve examination, deep tendon reflexes, and muscle strength were normal. There were no pathological reflexes, ataxia or nystagmus. She walked independently without support. Meningeal signs were absent, and other systemic examinations were within normal limits. Her laboratory findings for blood and cerebrospinal fluid (CSF) examination were all in normal range, brain magnetic resonance imaging (MRI) and MR spectroscopy detected normal. Neurometabolic screening, repeated sleep EEGs were normal. Genetic analysis revealed homozygous mutation of TBC1D24 gene (NM_001199107):c.1499C>T (exon 7).

Case 2: He, sibling of the index case, was admitted to the neurology clinic at the age of 3 months with history of myoclonic jerks of lower limbs. His neurological examination, sleep EEG and cranial MRI were normal. Daily myoclonic seizures involving the face and extremities persisted despite the alternative combination of anti seizure medications. The sequencing analysis revealed same homozygous mutation of TBC1D24 gene. At the age of one, his neurological exam revealed moderate developmental delay. His myoclonic jerks of extremities were partially controlled under polytherapy.

Conclusions: Different epilepsy phenotypes associated with *TBC1D24* mutations have been described. These include familial infantile myoclonic seizure, progressive myoclonic epilepsy, epilepsy of infancy with migrating focal seizures, early infantile epileptic encephalopathy and epileptia partialis continua. Although different epilepsy syndromes are related to *TBC1D24* mutation, there are some common features of *TBC1D24*-related epilepsy. The most prominent clinical feature among epilepsy types was multifocal myoclonus. TBC1D24 mutation-causing epilepsy is mostly drug-resistant. The most effective antiepileptic drugs are valproic-acid combined with phenobarbital or clobazam. Ketogenic diet is one of the alternative treatment option. In conclusion, we discussed the clinical features and treatment efficacy of two siblings with familial myoclonic epilepsy associated with *TBC1D24* gene mutation.

References

1 Balestrini S, Milh M, Castiglioni C, et al.: TBC1D24 genotype-phenotype correlation: Epilepsies and other neurologic features. Neurology 2016;87:77–85

2 Ngoh A, Bras J, Guerreiro R, McTague A, Ng J, Meyer E, Chong WK, Boyd S, MacLellan L, Kirkpatrick M, Kurian MA. TBC1D24 Mutations in a Sibship with Multifocal Polymyoclonus. Tremor Other Hyperkinet Mov (N Y). 2017 Apr 13;7:452.