Two Cases of ACTL6B Mutation-Associated Epileptic Encephalopathy

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INTRODUCTION

The ACTL6B (Actin-Like Protein 6B) mutation causes a clinical syndrome called 'Developmental and epileptic encephalopathy 76' characterized by persistent seizures, epileptic encephalopathy, motor and mental developmental disorders that begin in the first days/weeks of life.

In this article, a 5-year-old boy and a 9-year-old girl presenting with microcephaly, psychomotor developmental delay and diffuse spasticity are presented. Whole exome sequencing (WES) identified in both patients a homozygous mutation in the ACTL6B gene.

CASE 1

A 2-year-old male patient presented with generalized tonic-clonic seizures, intellectual disability, and delayed speech.

Patient's first seizure started at the age of 18 days in the form of forward contractions and jerks. Phenobarbital (PHB) treatment was used for 2 months and stopped due to an increase in seizure frequency. Then vigabatrin was started. Valproic acid was added to the treatment of the patient whose seizures could not be controlled with the treatment.

Physical examination: Head circumference: 48 cm (<3p), reduced orientation and cooperation, no eye contact, object tracking and speech, axial hypotonia +, diffuse spasticity +, bilateral hyperactive DTRs, bilateral Babinski +, no clonus, scoliosis+.

- Cranial magnetic resonance imaging (MRI): Hydrocephalus (2 years).
- Electroencephalography (EEG): Multifocal spike-wave discharges originating from the right temporal and occipital region (3 years).
- Chromosome analysis: 46, XY.
- Microarray analysis: 929 kilobase duplications (15 markers) in the 12p12.3 region.
- Whole exome sequencing (WES): Homozygous c.85G>A mutation (AR) in the ACTL6B (NM_016188.4) gene.

CASE 2

A 6-year-old female patient presented with atonic, generalized tonic-clonic seizures, intellectual disability, inability to speak and walk.

The first seizures of the patient started when she was 5 years old as head drop and loss of tone in the body. Levetiracetam (LEV) treatment started in another center, and after 4 months, patient had complaints such as nervousness and restlessness, so LEV switched to carbamazepine (CBZ). When seizures continued under CBZ and new seizures began in generalized tonic clonic character, first valproic acid was added to the treatment, then CBZ was stopped and clobazam (CLB) was started.

Physical examination: Head circumference: 46 cm (<3p), reduced orientation and cooperation, no speech, bilateral hyperactive DTRs, bilateral Babinski +.

- Cranial MRI: Cerebral and cerebellar atrophy (8 years).
- EEG: Spike-multiple spike wave discharges originating from bilateral frontal and temporal regions (5 years).
- Chromosome analysis: 46, XX.
- Microarray analysis: Normal.
- WES: Homozygous c.1267C>T mutation (AR) in the ACTL6B (NM_016188.4) gene.

CONCLUSIONS

In the clinical syndrome called 'Developmental and epileptic encephalopathy 76', findings such as microcephaly, atypical facial appearance, cortical blindness, kyphoscoliosis, growth retardation, feeding difficulties can be seen in addition to the clinic mentioned before. Cerebral atrophy, hypomyelination, decreased white matter volume, and thinning of the corpus callosum can be seen on brain magnetic resonance imaging (MRI). The ACTL6B gene is located on the 7th chromosome (7q22.1) and its mutations are inherited as autosomal recessive and autosomal dominant. In Case 1, the homozygous c.85G>A mutation in the ACTL6B gene caused early onset seizures in line with the typical clinic, while the homozygous c.1267C>T mutation in Case 2 had a milder course and the seizures started later. Different mutations in the ACTL6B gene may cause different clinical presentations.

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