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A Case of *PLA2G6*-Associated Neurodegeneration with Frequent Myoclonus and Generalized Onset Tonic–Clonic Seizures: Successful Treatment with Zonisamide

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Dear Editor,

Phospholipase A2 group VI (*PLA2G6*)-associated neurodegeneration (PLAN) is classified into four clinical subtypes: infantile neuroaxonal dystrophy (INAD), atypical neuroaxonal dystrophy (ANAD), adult-onset dystonia parkinsonism, and autosomal recessive early-onset parkinsonism.[1] ANAD has an age at onset ranging from 3 years to late teens, and is accompanied by symptoms of ataxia, rigidity, spasticity, and myoclonic epilepsy.[1,2] Progression is slower for ANAD than for INAD. We report the case of a Korean patient with genetically confirmed ANAD who presented with progressive spastic paraplegia and myoclonic epilepsy. We discuss the seizures that occur in ANAD patients, which were successful treated by zonisamide in the present case. This case has been reported in the spastic paraplegia case series by Kim et al.,[3] but the present paper focuses on the clinical features and treatment of seizures.

A 33-year-old male visited our epilepsy center for the management of recently aggravated myoclonus and generalized tonic–clonic seizures (GTCS). He was born at full term via a normal delivery. There was no family history of neurological problems. The patient reported that his spastic gait had begun at the age of 14 years and had gradually progressed. He was diagnosed with spastic paraplegia at the age of 23 years, and myoclonic seizures had appeared within the year prior to the diagnosis. Whole-genome sequencing analysis was performed at an age of 31 years, which revealed the following novel variants in *PLA2G6* that were shown to be biallelic: NM_003560.2:c.(278C>A); NP_003551.2:p.(Pro93His) and NM_003560.2:c.(1634A>G); NP_003551.2:p.(Lys545Arg).[3] The variants were classified according to the American College of Medical Genetics and Genomics 2015 criteria. Segregation analysis showed that the NM_003560.2:c.(1634A>G) mutation was of paternal origin, and confirmed the mother as a carrier of the NM_003560.2:c.(278C>A) mutation.

The onset of seizures occurred when the patient was 22 years of age, and he experienced a few GTCS annually up to the age of 32 years, at which time he visited a different hospital due to seizure aggravation, and was prescribed levetiracetam and topiramate. However, he experienced severe side effects of somnolence and cognitive decline, and so discontinued all antiepileptic medications. He subsequently visited the present epilepsy center for the management of frequent myoclonus and an increased frequency of GTCS (two or three times monthly).

A neurological examination revealed bilateral lower limb spasticity, distal dominant weakness (Medical Research Council grade 4), and hyperreflexic knee jerks. The perception of vibration and proprioception were impaired in the lower limbs. In addition, the patient demonstrated gait disturbance with bilateral limb ataxia on finger-to-nose and heel-to-shin testing, but he had no parkinsonian features.

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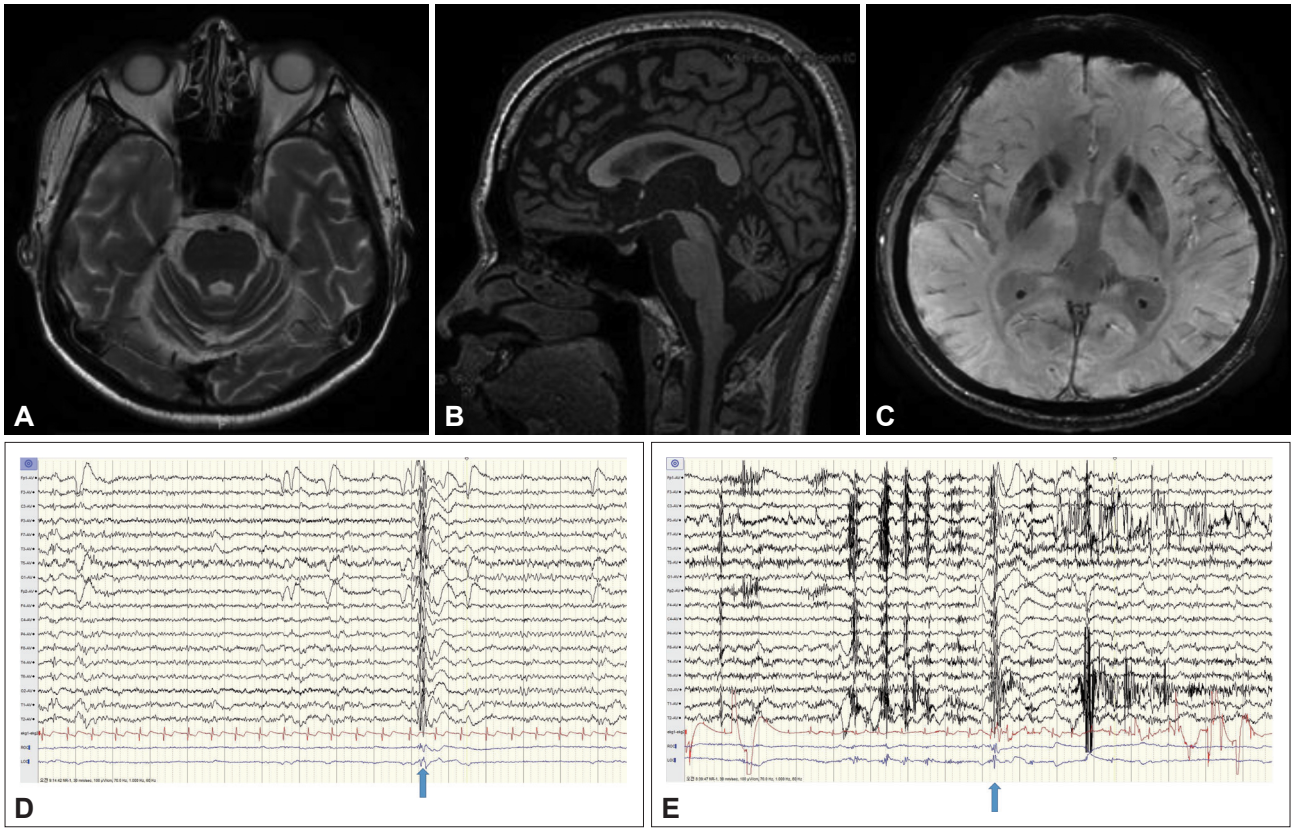

Fig. 1. Ictal EEG and brain MRI. A: Axial T2-weighted MRI demonstrating prominent cerebellar atrophy. B: Sagittal T1-weighted MRI demonstrating cerebellar atrophy. C: Axial gradient recalled echo T2-weighted MRI showing iron deposition involving the globus pallidus. D: Interictal EEG demonstrating interictal generalized polyspike-and-wave discharges (arrow). E: Ictal EEG demonstrating generalized polyspike-and-wave discharges during myoclonic movements over the bilateral upper extremities (arrow).

Brain MRI performed on admission revealed prominent cerebellar atrophy and iron deposition involving the globus pallidus and substantia nigra (Fig. 1A, B, and C). Video EEG monitoring revealed interictal multifocal spikes and frequent generalized polyspike-and-wave discharges (Fig. 1D). Myoclonus was detected very frequently (Fig. 1E). Most of the myoclonic seizures were not accompanied by ictal discharges, but some of them were evidently accompanied by generalized polyspikes. GTCS were not detected during monitoring.

The patient was treated with zonisamide at 50 mg b.i.d. and experienced a marked reduction in myoclonus and GTCS. He remained free of GTCS for 6 months after the medication dose was increased to 100 mg b.i.d.

To the best of our knowledge, diagnosing PLAN is difficult (especially the ANAD subtype) due to atypical clinical symptoms. Our patient exhibited spastic paraplegia, cerebellar ataxia, and myoclonic epilepsy. It was difficult to determine the efficacy of levetiracetam and topiramate because the treatment had been discontinued due to side effects; however, zonisamide was found to relieve myoclonus and GTCS without any severe adverse effects. Zonisamide is an antiepileptic drug used to control several types of seizures (including myoclonus) and has been proposed to be effective in the management of myoclonus-dystonia.[4] Furthermore, zonisamide exerts smaller effects on cognition, mood, and inducing sleep compared with levetiracetam and topiramate.

We have reported successful seizure control with zonisamide in a patient with PLAN (ANAD subtype) demonstrating symptoms of spastic paraplegia and myoclonic epilepsy.

Author Contributions

Conceptualization: Hye-Jin Moon. Writing—original draft: Hye-Jin Moon, Hongchul Ahn. Writing—review & editing: Hye-Jin Moon, Beomseok Jeon.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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REFERENCES

1. Guo YP, Tang BS, Guo JF. PLA2G6-associated neurodegeneration (PLAN): review of clinical phenotypes and genotypes. *Front Neurol* 2018;9:1100.
2. Cif L, Kurian MA, Gonzalez V, Garcia-Ptacek S, Roujeau T, Gelisse P, et al. Atypical PLA2G6-associated neurodegeneration: social communication impairment, dystonia and response to deep brain stimulation. *Mov Disord Clin Pract* 2014;1:128-131.
3. Kim A, Kumar KR, Davis RL, Mallawaarachchi AC, Gayevskiy V, Minoche AE, et al. Increased diagnostic yield of spastic paraplegia with or without cerebellar ataxia through whole-genome sequencing. *Cerebellum* 2019;18:781-790.
4. Hainque E, Vidailhet M, Cozic N, Charbonnier-Beaupel F, Thobois S, Tranchant C, et al. A randomized, controlled, double-blind, cross-over trial of zonisamide in myoclonus-dystonia. *Neurology* 2016;86:1729-1735.