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A Case of Intractable Startle-Induced Epilepsy Improved with a Low Dose of Perampanel

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Abstract

We report a 23-year-old man with intractable startle-induced epilepsy. The most annoying symptom was a partial startle-induced seizure resulting in falling. Multiple antiepileptic drugs showed no efficacy to startle-induced seizures. However, only 1 mg of perampanel (PER) at bedtime decreased his startle-induced seizures dramatically without any adverse events. PER, even though a low dosage could be effective for intractable startle-induced epilepsy.

Keywords: Startle-induced epilepsy; Perampanel

Introduction

Startle-induced epilepsy was firstly described by Alajouanine T and Gastaut H in 1955. It is one of the reflex seizures and most of the patients suffer from falling; however, startle-induced seizures are generally refractory to antiepileptic drugs (AEDs) and the standard approach has not been established yet [1-3]. Perampanel (PER), a non-competitive and selective α-amino-3-hydroxy5-methyl-4-isoxazolepropionic acid (AMPA) receptor antagonist, is one of the novel AEDs with a good efficacy for focal epilepsy and an acceptable tolerability. Here we present a patient of intractable startle-induced epilepsy improved dramatically with the addition of a low dose of PER.

Case Report

We present the case of 23-year-old Japanese man without a remarkable family history. He was born out of a non-consanguine marriage. He was diagnosed as West syndrome in 6 months of age because he developed infantile spasms. As he grew up, he presented frequent startle-induced seizures resulting in falling, frequent myoclonus in limbs, rare generalized tonic-clonic seizures, and a moderate mental retardation. Routine laboratory examination was normal. Brain MRI demonstrated the old vascular lesion in right basal ganglia with surrounding atrophy. Interictal SPECT revealed the reduction of cerebral blood flow in the right hemisphere, especially in the frontal lobe. Interictal EEG showed a vertex polyspikes or spike-and-wave discharges (**Figure 1**).

Generalized tonic-clonic seizure disappeared after administration of Carbamazepine (CBZ) and Sodium Valproate (VPA), and myoclonus decreased significantly by the addition of Diazepam (DZP). However, startle-induced seizures were intractable. Levetiracetam (LEV) and Clonazepam showed no efficacy for startle-induced seizures and he could not be tolerated with the daytime drowsiness. The reason why Clobazam (CLB) and Lamotrigine (LTG) had not been administered was not informed.

He referred to Shonan Fujisawa Tokushukai Hospital at 21 yrs of age with a regimen of CBZ 600 mg, VPA 800 mg, and DZP 2 mg daily. He presented mental retardation, agnosia, and apraxia. Although he presented a mild left-sided spastic hemiparesis, he could walk by himself. Neither deformities nor skin nodules were observed. Startle-induced seizures caused falling every day, which interfered with his daily activities severely. Concerned about the daytime sleepiness, he and his family did not select the addition of CLB. The increase of VPA to 1100 mg daily showed no efficacy for startle-induced seizures. Therefore, we added 1 mg of PER at bedtime and achieved the remission of startle-induced seizures immediately without any adverse events. Over a six-month period, startle-induced seizures decreased to once a month at most.

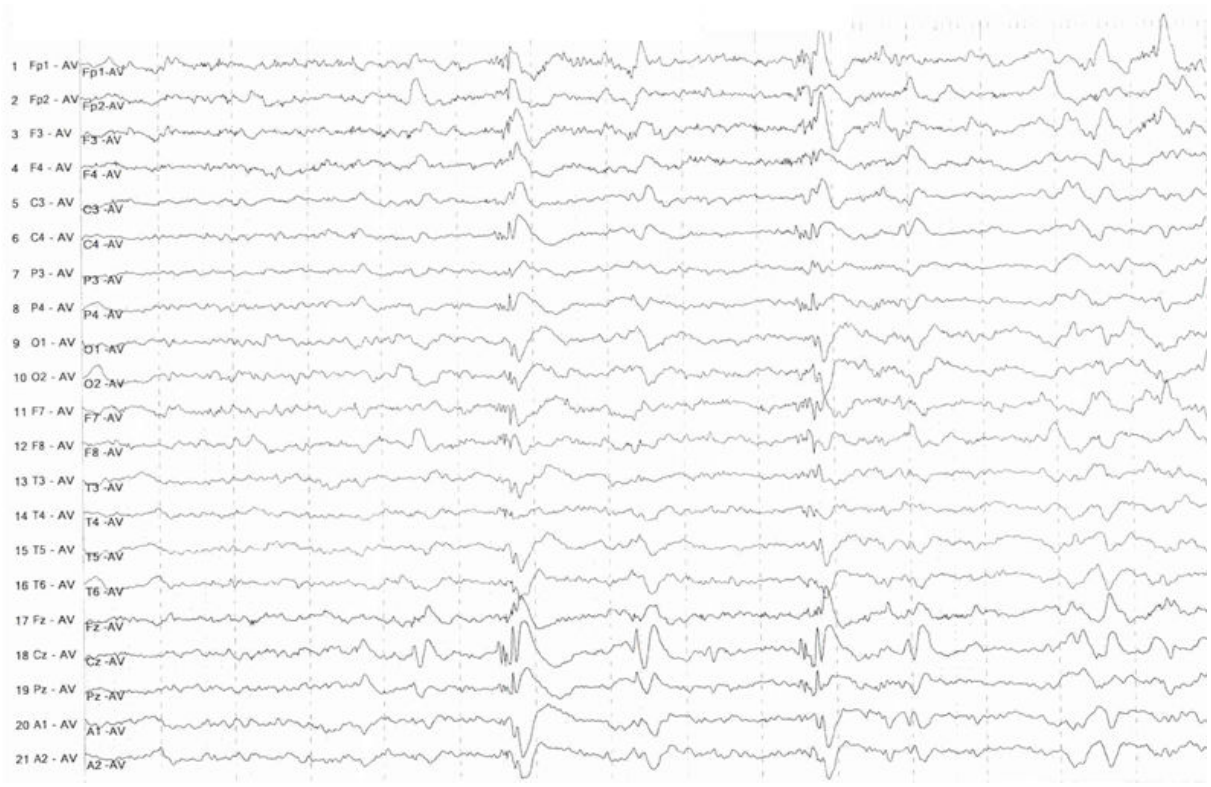

Figure 1: Interictal EEG showed a vertex polyspikes-and-wave complex before the administration of PER.

Discussion

Reflex seizures are triggered by some specific stimulation such as vision, non-verbal cognition, reading, music, eating, movement, somatosensory, hot water, and orgasms. Startle-induced epilepsy is a rare form of reflex seizures triggered by unexpected or surprising sensory stimulus, which are usually acoustic. The characteristic of startle-induced seizures is partial with a short duration within 30 s; however, falling is common if seizures occur in standing [2,3]. Some AEDs, such as CLB [2,4], LTG [5,6], and LEV [7], have been reported to be effective for startle-induced epilepsy; however, standard antiepileptic treatment has not been established yet.

PER is one of the new AEDs developed by Eisai Co. Although the exact antiepileptic mechanism of PER in human has not been elucidated, the antagonism of AMPA receptor was suggested to suppress neuronal hyperexcitability leading to the anticonvulsant effects. In fact, PER shows a good efficacy for focal epilepsy with an enough safety and tolerability. It is currently approved in more than 50 countries as adjunctive treatment for partial-onset seizures with or without secondarily generalized seizures and primary generalized tonic-clonic seizures in patients with epilepsy 12 yrs of age and older [8]. Moreover, the U.S. Food and Drug Administration expanded the indication for partial-onset seizures in pediatric patients with epilepsy 4 yrs of age and older in 2018. Additionally, PER was focused as a candidate agent for sporadic amyotrophic lateral sclerosis because it might prevent neuronal death by improvement of the increased Ca^{2+} influx [9].

The process of administration of PER depends on whether enzyme-inducing AEDs, including CBZ, oxcarbazepine, and phenytoin are combined or not. For adolescent or adult patients of epilepsy without enzyme-inducing AEDs, 2 mg at bedtime is recommended as an initial dose. The recommended maintenance dose ranges 8 mg to 12 mg at bedtime with titration of 2 mg daily at weekly intervals. On the other hand, for patients with enzyme-inducing AEDs, the maximum dose is 12 mg at bedtime with the similar titration. However, it is recommended to start PER from 4 mg at bedtime because an enzyme-inducing AEDs may reduce the serum concentration of PER by increasing its clearance. In either case, it is important to titrate PER slowly for minimizing adverse events including dizziness, somnolence, and headache [8,10-12]. Thus, we added PER from a low dosage to avoid the occurrence of these adverse events, although a larger amount of PER could be necessary in future.

It was suggested that AMPA receptors were involved in posthypoxic myoclonus in animal experiment with rats [13]. Furthermore, several reports about the effectiveness of PER for progressive myoclonus epilepsy syndrome including Lafora disease [14-16], dentatorubral-pallidoluysian atrophy (DRPLA) [17], Unverricht–Lundborg disease [18] and sialidosis [19] were published. In addition, PER was reported to be effective for hypoxic myoclonic status or *Lance-Adams syndrome* [20,21]. These basic and clinical reports suggested *that PER has some potential* to myoclonic epilepsy and cortical myoclonus. The mechanism of reflex epilepsy has not been well understood; however, reflex traits are predominantly seen in patients with

genetic myoclonic epilepsy [22]. To our knowledge, this is the first case of startle-induced epilepsy presenting a beneficial efficacy of PER. PER might have some potential to startle-induced epilepsy and we have to continue further considerations with more patients to prove the efficacy of PER for startle-induced epilepsy.

Conclusion

PER is the one of the novel AEDs with unique mechanism. It may be effective for intractable startle-induced epilepsy. Further investigations with more patients should be necessary.

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Conflicts of Interest

There are no conflicts.

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