The efficacy of lamotrigine for atypical absence status epilepticus in a case of perioral myoclonia with absence

Yusuke Takezawa¹,², Yosuke Kakisaka²,³, Keisuke Wakusawa², Mamiko Ishitobi², Naomi Hino-Fukuyo², Takehiko Inui¹, Wakaba Endo¹, Mai Anzai¹, Nobukazu Nakasato³, Kazuhiro Haginoya¹,²

¹Department of Pediatric Neurology, Takuto Rehabilitation Center for Children, Sendai 982-0241, Japan
²Department of Pediatrics, Tohoku University School of Medicine, Sendai 980-8574, Japan
³Department of Epileptology, Tohoku University Graduate School of Medicine, Sendai 980-8574, Japan

Key words: Perioral myoclonia, Absence, Generalized epilepsy, Atypical absence status epilepticus, Axial tonic seizure

Received: November 6, 2015; Accepted: August 26, 2016; Published online: October 28, 2016

Abstract

Perioral myoclonia with absences, which is currently not recognized officially by the International League Against Epilepsy classification, is generalized epilepsy characterized by short absences with constant rhythmic contraction of the perioral muscles. The long-term outcome and features of this disease are not clear. We describe a patient with perioral myoclonia with absences, brief axial tonic seizures, and atypical absence status epilepticus, who was followed for 21 years. The efficacy of lamotrigine in this case was remarkable. This report suggests that when clinicians see a patient with absences accompanied by myoclonia limited to the facial area, perioral myoclonia with absences should be considered in terms of appropriate treatment and care for atypical absence status epilepticus.
Introduction

Perioral myoclonia with absences (PMA) is an epilepsy syndrome first described in 1994 by Panayiotopoulos et al. [1], which is currently not officially recognized by the International League Against Epilepsy (ILAE) classification [2]. This syndrome is generalized epilepsy characterized by short absences with pronounced, constant rhythmic contraction of the perioral muscles mainly involving the orbicularis oris, with variable alterations in consciousness [1]. PMA has also been reported to have a normal neurological status, normal electroencephalography (EEG) background activity with generalized spike-waves or polyspike-waves around 3–4 Hz during seizures, poor response to antiepileptic drugs, and atypical absence status epilepticus (ASE) occurring in most patients [1, 3, 4]. However, there are no reports on the long-term outcome of these seizures. Here, we describe the clinical and polygraphic recording features of a patient with PMA who also had brief axial tonic seizures and atypical ASE, during 21 years of follow-up.

Case Report

A 27-year-old Middle Eastern male patient had a normal antenatal and perinatal medical history, and his psychomotor development was normal. He never had febrile convulsions, and his family history was unremarkable. At 6 years of age, he had generalized tonic-clonic seizure and began to experience absence seizures from a few times daily to weekly. He was diagnosed with epilepsy based on abnormal EEG findings and treated with anticonvulsants including phenobarbital (PB), ethosuximide (ESM), and primidone. Subsequently, generalized tonic-clonic seizures (GTCs) disappeared, but the absence seizures were not controlled. When he was 10 years of age, GTCs recurred, and he had brief episodes of twitching of the left-side of the mouth and right shoulder. From the age of 12, absence seizures remitted for 3 years after medications were adjusted, until he moved to Japan with his family. At age 15, he was referred to our hospital because of an increased frequency of absence seizures ranging from once weekly to daily. Nevertheless, his high school performance was excellent. At that time, he was treated with valproate (VPA) (400 mg/day) and lamotrigine (LTG) (50 mg/day). Video-EEG was recorded with surface electromyography over the left orbicularis oris muscle, right deltoid muscle, and right trapezius muscle. He had normal background activity during wakefulness and sleep. A few absence seizures associated with repeated contraction of the left orbicularis oris muscle or right shoulder were recorded. The ictal EEG showed irregular 2–3 Hz spikes or polyspikes and slow wave bursts over bilateral frontal areas (Fig. 1a). Interictal bilateral spike-waves and polyspike-waves were also recorded, which were predominant over bilateral frontal-central areas (Fig. 1b). At age 16, since LTG was not approved in Japan at that time and the patient's father had to import the drug by himself, we tried to replace LTG...
with other antiepileptic drugs [ethosuximide (ESM) and clobazam (CLB)] with consent from the patient and his family. Subsequently, the frequency of GTCs increased to once a week and his family noticed that his concentration decreased and he seemed to be sleepy. We therefore discontinued ESM the next month. Unfortunately, GTCs were not controlled, and his concentration and drowsiness worsened. Brief axial tonic seizures were also observed around this time. Two months after discontinuing LTG, GTCs occurred daily, which were preceded by massive myoclonic seizures. Although addition of PB decreased the frequency of GTCs slightly, his performance in high school deteriorated, and he began to show slow response to the surroundings. He was admitted to our hospital with suspected atypical ASE. At the time of admission, he was treated with VPA (1000 mg/day), PB (60 mg/day) and clobazam (15 mg/day). Physical examination on admission was normal. Blood tests including thyroid function, antinuclear antibody, and amino acid analysis were within normal ranges. He had moderately low scores on the Wechsler Intelligence Scale for Children-III (full-scale IQ 67, verbal IQ 77, performance IQ 62). The other findings were unremarkable, including brain fluorine-18 fluorodeoxyglucose positron emission tomography, brain single photon emission computed tomography, and brain magnetic resonance imaging. The EEG showed continuous generalized irregular 2–3 Hz spike-waves bursts during wakefulness, which was considered atypical ASE (Fig. 2).

This abnormal finding fluctuated depending on mental workload. In this tracing, no myoclonus or brief axial tonic seizure was observed. Since clinical deterioration was apparently related to discontinuation of LTG, LTG was restarted at 50 mg/day, which resulted in prompt reduction in GTCs and improvement of concentration and responsiveness. At the time of discharge, the dose was increased to 100 mg/day, and absence seizures decreased while no brief axial tonic seizures were observed. Four months later, LTG was increased to 150 mg/day, and PB was discontinued. His performance in high school recovered completely.

When he was 18 years of age, interictal EEG showed no paroxysmal discharge. Although absence seizures occurred weekly and GTCs monthly to yearly, he continued to perform well in school and passed the college entrance examination in his home country, where he stayed during his college years. Recently, he started postgraduate studies at a university in Japan and has been prescribed VPA (1000 mg/day), LTG (100 mg/day), levetiracetam (1500 mg/day), and CZP (1 mg/day) by another clinic because he has been far away from our hospital. He has had no GTCs in the last two years but still experience absence seizures weekly.

**Discussion**

The clinical features of this patient were consistent with those of PMA [1], such as brief episodes of absences with perioral myoclonia, infrequent GTCs, occurrence of atypi-
cal ASE, normal neurological development, childhood onset, and video-EEG findings. Poor response to antiepileptic drugs for absences with perioral myoclonia is also compatible with PMA. Facial myoclonic manifestations associated with generalized spike and wave components have been reported in childhood absence epilepsy (CAE), epilepsy with myoclonic absences (EMA), eyelid myoclonia with absences (Jeavons syndrome), juvenile myoclonic epilepsy (JME), Lennox–Gastaut syndrome (LGS), and PMA [5-9]. In CAE, perioral myoclonia is present in some cases but is not pre-eminent, and ictal EEG and prognosis are different from those reported for PMA [5] and in our patient. In EMA, myoclonia may involve facial muscles but predominates in the shoulders and arms. Although the age of onset and intractability of seizures are similar to those of our patient, the presence of intellectual disability and EEG findings characterized by 3 Hz spike and wave in ASE [6] differ from those in our patient. Jeavons syndrome is characterized by jerking of the eyelids, often associated with jerky upward deviation of the eyeballs and retropulsion of the head [7], which are different from the manifestations of our patient. JME may also exhibit facial myoclonia, generalized slow poly-spike-waves and general tonic-clonic seizures. However, the age of onset (mainly teens), good response to antiepileptic drugs and low frequency of absences [8] do not match the features of our patient. LGS is one of the most probable diagnosis, because the patient had generalized slow (≤ 2.5 Hz) spikes and waves, atypical ASE, poor response to treatment, tonic seizures, atypical absence, and possible facial myoclonia. Nevertheless, some of the hallmarks of Lennox–Gastaut syndrome were missing in our patient, such as bursts of generalized fast polyspike (10–20 Hz) during sleep, an abnormal waking EEG background, “drop attacks”, cognitive impairment, and an identifiable cause [9]. From these points of view, we believe that our patient most likely has PMA. In general, a diagnosis of PMA allows us to predict the prognosis and efficacy of antiepileptic drugs. In addition, atypical ASE may be a clue for a diagnosis of PMA [3]. According to previous case reports, VPA, ESM, LTG and topiramate are sometimes effective, while worsening seizures have been reported after adding carbamazepine or ox-carbazepine [1, 4, 10-14]. In our case, the response to LTG was impressive. In addition, brief axial tonic seizures were observed during a period when ASE occurred, which had not been reported before.

In conclusion, our 21-year follow-up indicates that cognitive impairment does not progress in PMA despite uncontrolled absence seizures, which imply that it is not caused by epileptic encephalopathy. When clinicians see a patient with absences with myoclonia limited to the facial area, a polygraphic investigation is necessary to obtain the correct diagnosis, and atypical ASE should be considered.

References

[1] Panayiotopoulos CP FC, Giannakodimos SE, Robinson RO. Perioral myoclonia


Fig. 1. Video-electroencephalography (EEG) recordings. (a) Ictal EEG shows generalized irregular 2–3 Hz spikes or polyspikes and slow waves bursts over the bilateral frontal areas associated with repeated contractions of the left orbicularis oris muscle. (b) Interictal video-EEG shows bilateral spike-waves and polyspike-waves, with irregularities in number and amplitude of spikes in the spike-wave complex, which are predominant over the bilateral frontal to central areas. R. Delt.: right deltoid muscle; R. Traps.: right trapezius muscle; L. Orb. Or.: left orbicular oris muscle.
Fig. 2. Electroencephalography (EEG) during atypical absence status epilepticus. EEG shows continuous, generalized 2.5–3 Hz spike-waves and polyspike-waves during the waking state. During this state, his responsiveness was slow.
Fig. 3. Clinical course of the present case. CLB, clobazam; VPA, valproic acid; PB, phenobarbital; ESM, ethosuximide; LTG, lamotrigine; GTCs, generalized tonic-clonic seizures.