Epilepsy & Behavior 25 (2012) 192–195

Contents lists available at SciVerse ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Case Report

A case of autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) coexisting with pervasive developmental disorder harboring *SCN1A* mutation in addition to *CHRNB2* mutation

Daichi Sone [a,*], Takayuki Sugawara [b], Eisuke Sakakibara [a], Yu Tomioka [a], Go Taniguchi [a], Yoshiko Murata [a], Masako Watanabe [a], Sunao Kaneko [b]

[a] *Department of Psychiatry, National Center of Neurology and Psychiatry, Japan*
[b] *Department of Neuropsychiatry, Graduate School of Medicine, Hirosaki University, Japan*

ARTICLE INFO

Article history:
Received 13 June 2012
Revised 27 July 2012
Accepted 28 July 2012
Available online 29 September 2012

Keywords:
Autosomal dominant nocturnal frontal lobe epilepsy
Pervasive developmental disorder
Autistic spectrum disorder
SCN1A
CHRNB2
Refractory epilepsy
Genetic epilepsy

ABSTRACT

We report a case of autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) with several characteristics distinct from previously reported cases, in which genetic studies identified mutations in two different genes. This case differed from typical ADNFLE with respect to the following: (1) slightly younger onset and refractory to antiepileptic drugs and (2) borderline intellectual functioning and coexistence of pervasive developmental disorder from infancy. Genetic testing revealed a novel mutation and a silent substitution in *SCN1A* (c.4285G>T, A1429S and c.4371G>C, silent) in addition to a known mutation in *CHRNB2* (c.1200C>G, I312M). *SCN1A* is a gene that codes for the voltage-dependent sodium channel α1 subunit and has been implicated in generalized epilepsy with febrile seizures plus and severe myoclonic epilepsy in infancy. However, the relation between SCN1A and ADNFLE is unknown. We report the clinical course and symptomatic characteristics of this case although the relationship between ADNFLE mutation and *SCN1A* mutation remains to be elucidated.

1. Introduction

Autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) was first reported in 1994 by Scheffer et al. [1] from Australia, as the first partial epilepsy to follow single gene inheritance. Most cases have infantile onset, which continues through to adulthood. The epilepsy is characterized by clusters of brief partial motor seizures during non-REM sleep. In recent years, mutations in the CHRNA4 and the CHRNB2 genes have been reported, leading to alterations in nicotinic acetylcholine receptor subunits. We report here a case of ADNFLE with clinical characteristics distinct from typical ADNFLE cases, and in which genetic testing detected mutations in two different genes.

2. Case report

An 18-year-old man was referred to our hospital with nocturnal tonic seizures of four extremities.

The patient had no remarkable past history including febrile convulsion. His father had similar seizures characterized by arm and leg extension at night and continued to have seizures around once a week while on antiepileptic drug treatment. The family tree of the patient shows that apart from the father, no other family members have documented seizure symptoms (Fig. 1). The patient had no documented neonatal abnormalities and no developmental abnormalities during regular infant and childhood health examinations. However, he had continuously displayed an autistic tendency. Since infancy, he did not make eye contact with others, had taken no interest in other persons, and played by himself. He also formed strong attachments to objects such as bedding and stuffed toys. Although his school performance was not good, he managed to pursue regular classes and graduated from a commercial high school. Thereafter, he had not been able to hold down a job and was helping with the family business. He was preoccupied with motor car catalogs but was not interested in other persons. The first seizures occurred around 3 years of age. The seizures occurred between nighttime and early morning, manifesting tonic extension of four limbs, with eyes open and eyeballs fixed centrally. He was conscious during all the seizures and had memories of them. Seizures occurred only during sleep, commonly before dawn, and lasted 10 to 20 s. The patient could wake up 5 to 6 times during the night due to seizures. The seizures never progressed to secondarily generalized seizures. From around 5 years of age, he had been treated with antiepileptic drugs, which failed to control the

* Corresponding author at: National Center of Neurology and Psychiatry, 4-1-1 Ogawa-Higashi, Kodaira, Tokyo 187-8551, Japan. Fax: +81 042 344 6745.
E-mail address: daichisone@gmail.com (D. Sone).

1525-5050/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.yebeh.2012.07.027

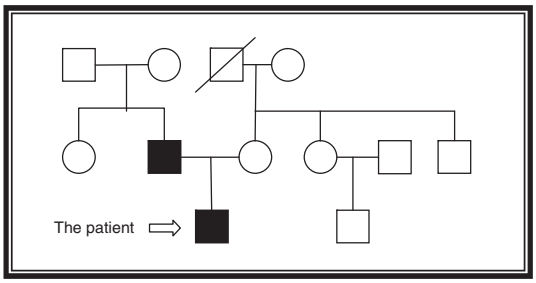

Fig. 1. The family tree of the patient. ■ denotes the individual with nocturnal seizure symptoms. The father of the patient had the same symptoms as the patient, but all other family members had no documented seizure symptoms.

seizures. The latest treatment regimen consisted of carbamazepine (CBZ) and sodium valproate (VPA). He was referred to our center for detailed examinations and treatment for the refractory seizures.

On admission, hematological and biochemical tests as well as urinalysis showed no abnormalities. Blood concentrations of antiepileptic drugs were 8.6 μg/ml for CBZ (therapeutic range: 4–12 μg/ml) and 60 μg/ml for VPA (therapeutic range: 50–100 μg/ml). Both waking and sleeping interictal EEG showed no definitive epileptic spikes, and background EEG was also normal. Hyperventilation and photostimulation elicited no abnormal waveforms. Magnetoencephalography also detected no spikes. Head MRI and interictal ECD-SPECT revealed no lesion that might constitute the epileptogenic zone. Electroencephalography-video monitoring recorded around five seizures per night. Tonic extension of four limbs and head rotation which lasted approximately 15 s were followed by recovery. Consciousness was not impaired during and after seizures, and palsy was not observed. All seizures were simple partial seizures, which manifested as focal motor seizures. There were left–right differences, but these differences varied from one seizure to another. All the recorded seizures occurred suddenly from stage II of nocturnal sleep. No seizure was recorded during an awake state. No specific abnormalities were detected on ictal EEG (Fig. 2). During hospitalization including the EEG-video monitoring period, the patient pleaded strongly to have his favorite bedding brought from home; otherwise, he was not able to spend the night in the hospital, and he was given permission to bring in his own bedclothes. On the Wechsler Adult Intelligence Scale (WAIS) III, his full scale IQ was 72, verbal IQ was 82, and performance IQ was 67. The scores showed borderline intellectual functioning and a significant discrepancy between verbal and performance IQs. The subscale scores

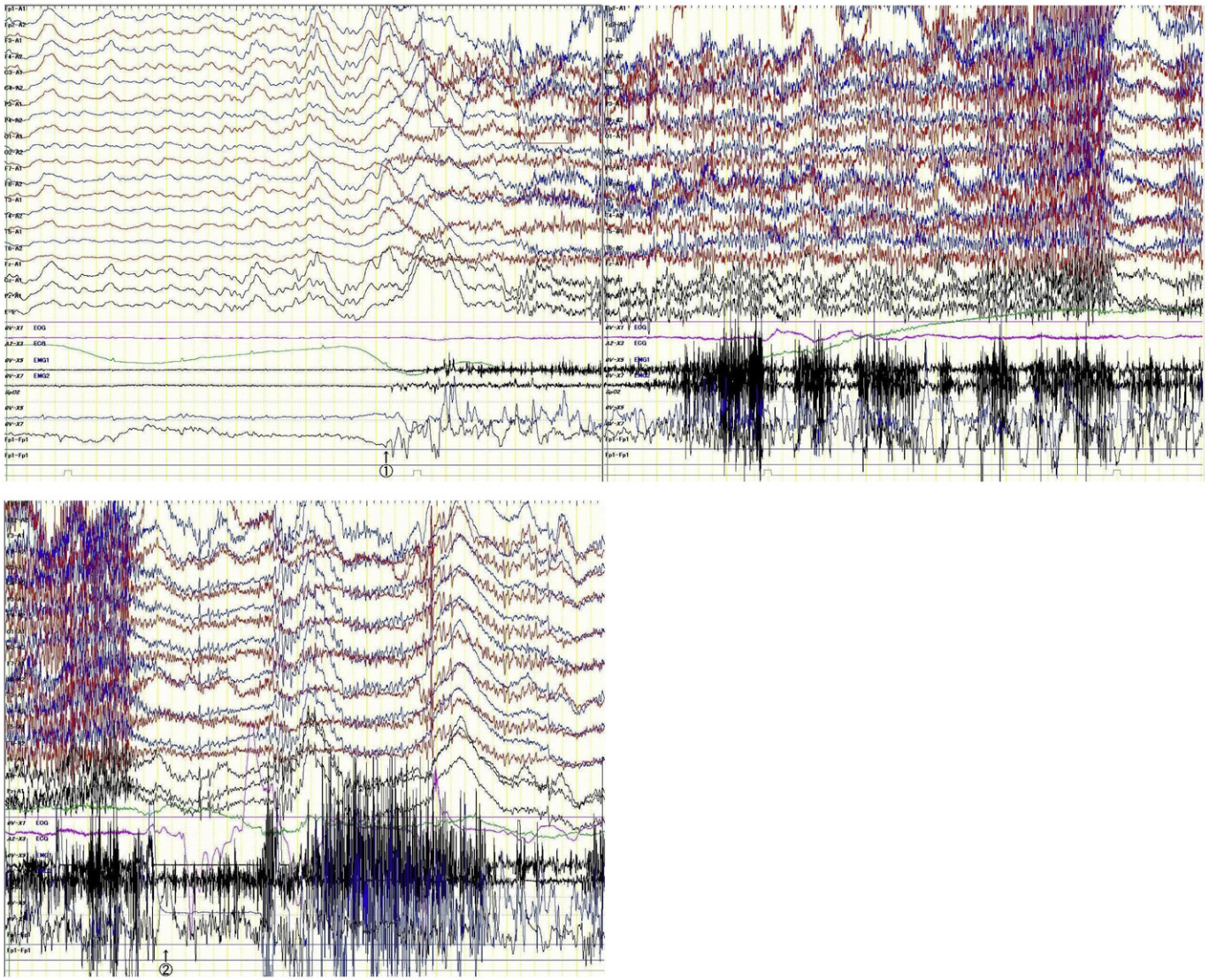

Fig. 2. Ictal EEG. From stage II sleep, the four limbs suddenly extend tonically (arrow ①), and seizure ends after around 15 s (arrow ②). Definitive epileptic discharge cannot be identified. The EEG was masked by large artifacts.