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Case Report

Focal seizures and epileptic spasms in a child with Down syndrome from a family with a *PRRT2* mutation

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Abstract

We describe a girl with Down syndrome who experienced focal seizures and epileptic spasms during infancy. The patient was diagnosed as having trisomy 21 during the neonatal period. She had focal seizures at five months of age, which were controlled with phenobarbital. However, epileptic spasms appeared at seven months of age in association with hypsarrhythmia. Upon treatment with adrenocorticotropic hormone, her epileptic spasms disappeared. Her younger brother also had focal seizures at five months of age. His development and interictal electroencephalogram were normal. The patient's father had had infantile epilepsy and paroxysmal kinesigenic dyskinesia. We performed a mutation analysis of the *PRRT2* gene and found a c.841T > C mutation in the present patient, her father, and in her younger brother. We hypothesized that the focal seizures in our patient were caused by the *PRRT2* mutation, whereas the epileptic spasms were attributable to trisomy 21.

Keywords: *PRRT2* mutation; Down syndrome; Benign infantile epilepsy; Epileptic spasms

1. Introduction

Down syndrome (DS) is the most common chromosomal abnormality syndrome observed in about 1 in 650–1000 live births [1]. The prevalence of epilepsy in DS ranges from 1–13% compared with 1.5–5% in the general population [2]. Infantile spasms are the most frequent epilepsy symptom in patients with DS, the outcome of infantile spasms is better in patients with DS than in those with other etiologies such as structural brain lesions and known genetic defects [1]. In contrast, focal epilepsy is rare in patients with DS.

Benign infantile epilepsy (BIE) is an autosomal, dominantly inherited epilepsy syndrome with an onset between three and twelve months of age. BIE seizures respond well to antiepileptic drugs, and remission occurs before the age of two years [3]. Mutations in the proline-rich transmembrane protein 2 (*PRRT2*) gene are frequently found in patients with BIE, infantile convulsions with choreoathetosis (ICCA), and paroxysmal kinesigenic dyskinesia (PKD) [4,5].

We describe a girl with DS who had focal seizures followed by epileptic spasms. Her younger brother experienced focal seizures with a favorable outcome, and her father had a history of ICCA. These facts prompted

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us to perform a mutation analysis of the *PRRT2* gene in this family. Here we present the clinical findings of our patient and her family, suggesting two seizure etiologies in one case.

2. Patients report

A 5-year-old girl was the first child of non-consanguineous healthy parents. She was born at full term weighing 2790 g by spontaneous vaginal delivery in good condition. After delivery, she was diagnosed with DS based on characteristic facial anomalies and esophageal atresia, which were surgically repaired twelve days after birth. Her karyotype was 47,XX,+21.

At five months, the patient had seizures characterized by loss of responsiveness, eye deviation, and cyanosis lasting for one minute. The seizures occurred in clusters, and she was admitted to our hospital. Her vital signs and physical and neurological examinations showed no abnormalities with the exception of generalized hypotonia. She could follow others' gaze and smile socially, but had poor head control. Her brain magnetic resonance imaging scan showed no abnormalities; however, the interictal electroencephalogram (EEG) revealed sporadic sharp waves in the left temporal area (Fig. 1a). Her seizures were controlled immediately with oral phenobarbital.

At six months, her parents noticed regression of psychomotor development. She gradually became apathetic and less responsive to her family. The EEG showed repetitive asynchronous high-voltage slow waves (Fig. 1b). Her treatment was changed from phenobarbital to valproic acid. At seven months, clusters of epileptic spasms appeared and her EEG showed hypsarrhythmia (Fig. 1c). She was diagnosed as having West syndrome and was treated with adrenocorticotropic hormone (ACTH), leading to immediate disappearance of epileptic spasms and hypsarrhythmia (Fig. 1d). Her developmental milestones recovered to those before epilepsy onset. The seizures did not recur, and valproic acid was discontinued at twelve months. The patient could sit without support at fifteen months

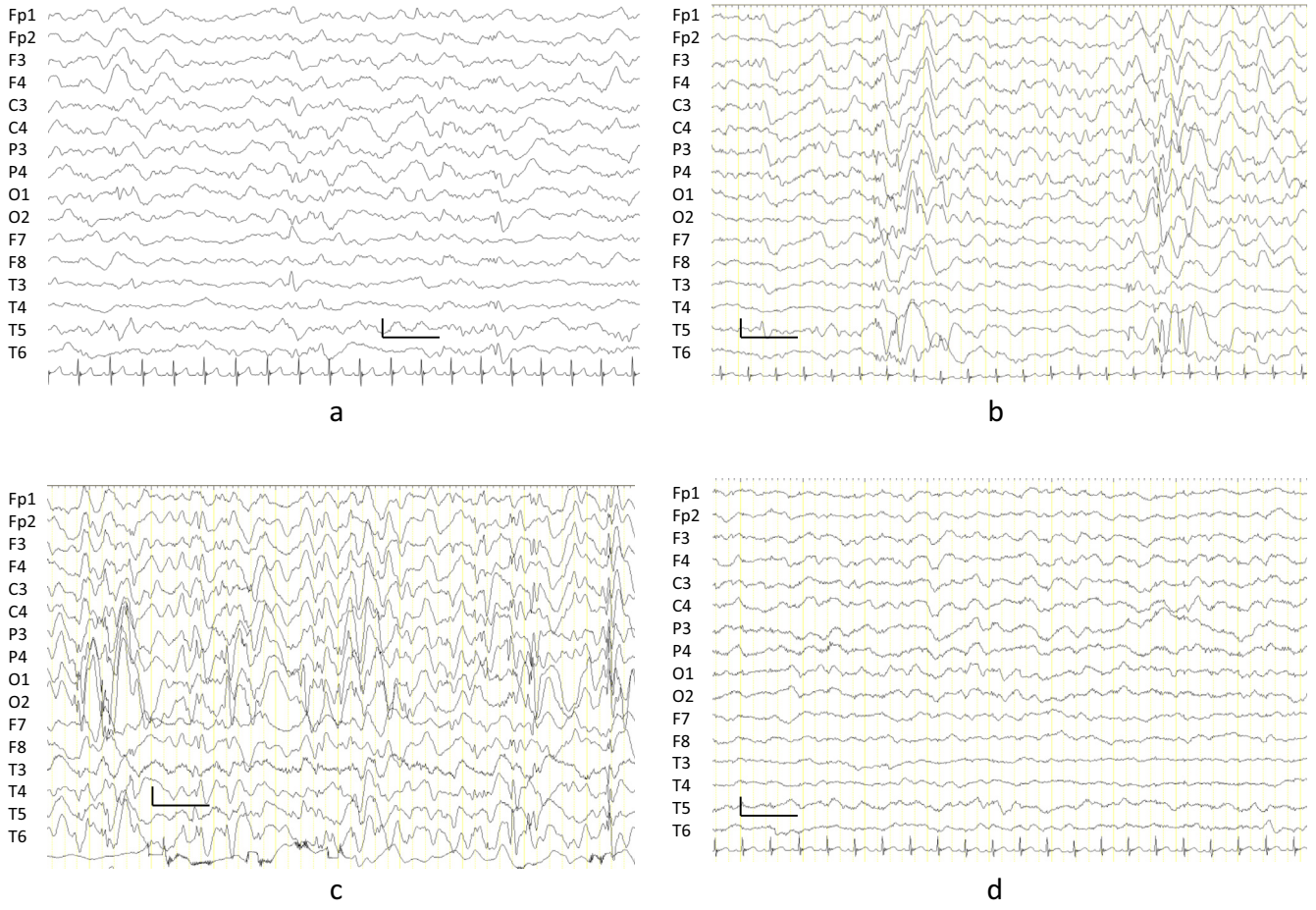

Fig. 1. Electroencephalographic (EEG) findings. (a) Sporadic sharp waves were observed in the left temporal area at five months of age. (b) At six months, repetitive asynchronous high-voltage slow waves were observed. (c) Hypsarrhythmia at seven months. (d) After administration of ACTH at nine months, hypsarrhythmia disappeared. Calibration: 100 μV, 1 s.