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Case Report

Dramatic response after functional hemispherectomy in a patient with epileptic encephalopathy carrying a *de novo COL4A1* mutation

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Abstract

We describe the first case of a successful functional hemispherectomy in a patient with epileptic encephalopathy and a *de novo* collagen type IV alpha 1 (*COL4A1*) mutation. A 4-year-old girl was *COL4A1* mutation-positive and suffered from drug-resistant epilepsy, hemiplegia, and developmental delay. Magnetic resonance imaging detected no porencephaly, and she had no cataract or renal abnormality. Following a presurgical evaluation for epilepsy, she underwent a functional hemispherectomy. She has been seizure free with no intracranial hemorrhage or other perioperative complications. Patients with a *COL4A1* mutation have an increased risk for intracranial hemorrhage because of disrupted integrity in the vascular basement membrane due to the mutation. After weighing the risks and benefits to these patients, epilepsy surgery may not be absolutely contraindicated. Furthermore, pediatric neurologists should be aware of an undiagnosed *COL4A1* mutation when a patient presents with an unexplained neurological phenotype, such as mild hemiparesis, even in the absence of porencephaly.

Keywords: COL4A1; Epileptic encephalopathy; Hemiplegia; Porencephaly; Infantile spasms; Functional hemispherectomy

1. Introduction

A collagen type IV alpha 1 (*COL4A1*) mutation can present in children as infantile hemiplegia/quadriplegia, stroke or epilepsy, or a motor disorder [1]. Yoneda et al. reported that porencephaly and other cerebrovascular diseases are often associated with ocular, renal, and muscular features in patients with a *COL4A1* mutation [2]; however, no clear genotype–phenotype correlation is present [3]. A case of infantile spasms with a *COL4A1* mutation was treated with antiepileptic drugs [1], although the semiology was not described in detail. Here, we report on the clinical course of a patient

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carrying a *de novo COL4A1* mutation associated with epileptic encephalopathy who was treated by functional hemispherectomy (FH).

2. Case

A 4-year-old girl was born at 41 weeks gestation after an uneventful pregnancy and delivery. Her weight, length, and head circumference at birth were 2636 g (−0.9 SD), 49.4 cm (+0.5 SD), and 33.5 cm (+0.3 SD), respectively. No family history of migraine, strokes, or cataracts was revealed.

Her parents noticed mild weakness in the left upper extremity during infancy, but her gross motor skills were normal. She experienced brief tonic seizures at about 6 months of age. Treatment with sodium valproate was initiated, but no improvement occurred. Soon thereafter, she was admitted to our hospital for further evaluation. A neurological examination showed microcephaly, mild left-sided hemiplegia, and deviation of the eyes to the right side. An ophthalmological examination showed no abnormalities, including cataracts. Brain magnetic resonance imaging (MRI) revealed enlarged bilateral lateral ventricles with increased periventricular signal intensity on T1-weighted and fluid-attenuated inversion recovery images, and decreased signal intensity on a T2-weighted image of the right periventricular wall (Fig. 1A–C). Her seizures were confirmed to be spasms by video-electroencephalography (EEG), and an inter-ictal EEG showed almost continuous irregular high voltage spikes and waves in right posterior quadrants (Fig. 1D). Based on these findings, we diagnosed this patient as West syndrome with hemihypsarrhythmia. A complete heart

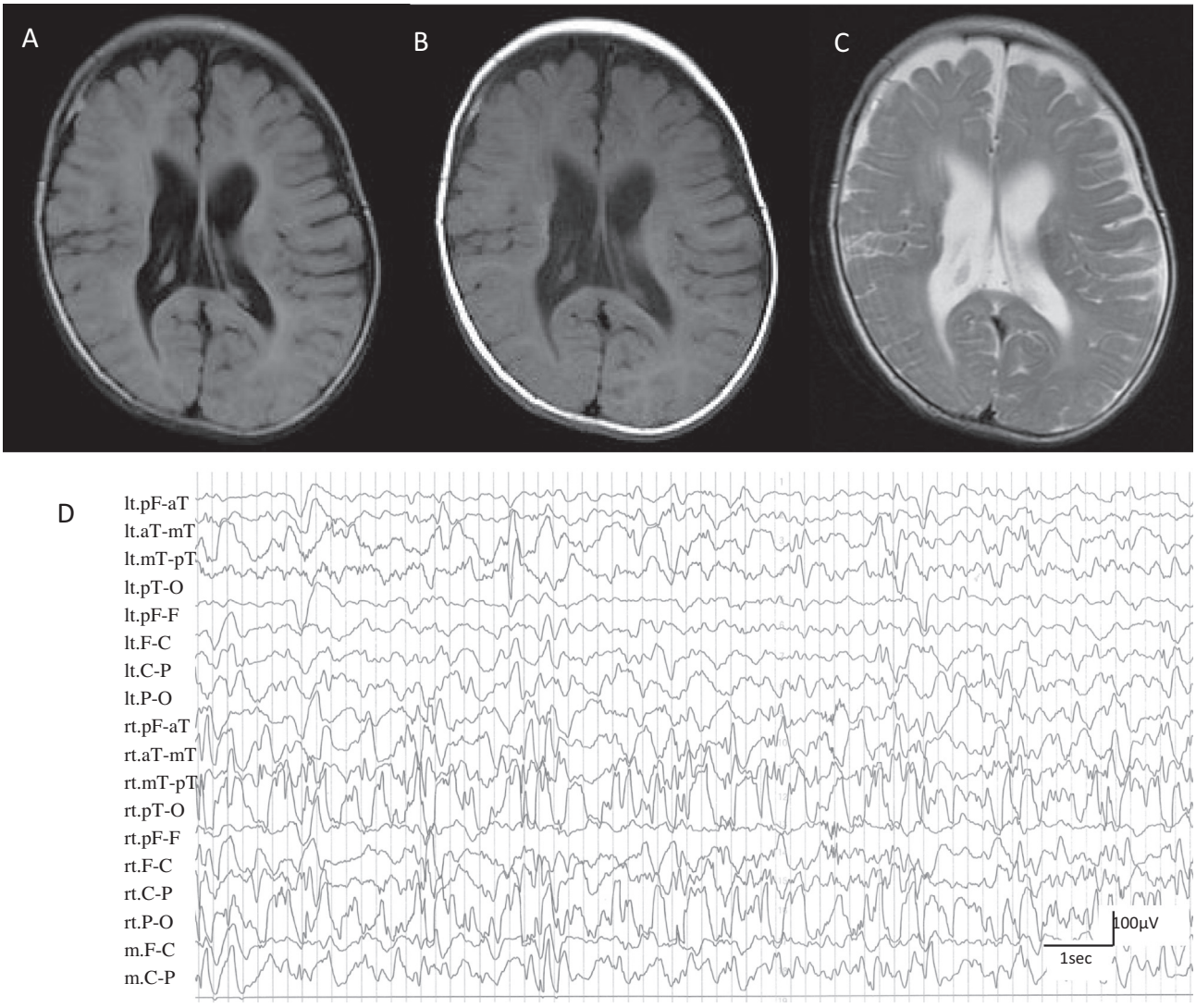

Fig. 1. Magnetic resonance imaging (MRI) and electroencephalogram (EEG) at 6 months of age. MRI (A: T1WI, B: fluid-attenuated inversion recovery [FLAIR], C: T2WI) shows a high signal intensity area in the right lateral ventricular wall on T1-weighted and FLAIR images, and decreased signal intensity on a T2-weighted image. Inter-ictal EEG shows almost continuous irregular high voltage spikes-and-waves in right posterior quadrants, which was considered hemihypsarrhythmia (D).