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Case Report

ATP1A3-related epileptic encephalopathy responding to ketogenic diet

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Abstract

Background: Alternating Hemiplegia of Childhood (AHC) is a rare neurological disease caused by mutations in ATP1A3 gene codifying for alpha3 subunit of Na^+-K^+ ATPase pump. Repeated and transient attacks of hemiplegia, usually affecting one side of the body or the other, or both sides of the body at once, are the core features of AHC. Monocular nystagmus, other abnormalities in ocular movements, dystonic posturing and epilepsy are commonly associated to AHC. However, the spectrum of ATP1A3 related diseases is still expanding and new phenotypes have been reported.

Case report: Here, we described a patient who developed a severe early onset drug-resistant epileptic encephalopathy and months later, he presented episodes of hemiplegic attacks and monocular nystagmus. Thus, AHC was hypothesized and a novel mutation in ATP1A3 gene was found. Interestingly, ketogenic diet (KD) was started and both epileptic seizures and classical AHC paroxysmal episodes stopped. Long-term follow-up shows a global improvement of neurological development.

Conclusions: Our case reinforces the role of KD as a novel therapeutic option for ATP1A3-related conditions. However, proper dedicated confirmatory trials on KD are necessary.

Keywords: ATP1A3; Ketogenic diet; Drug resistant epilepsy; Alternating hemiplegia of childhood

1. Introduction

ATP1A3 gene encodes for a subunit of the Na+/K+ ATPase pump. Mutations in ATP1A3 are responsible for a wild spectrum of highly disabling syndromes, with early childhood onset. ATP1A3-related conditions indeed include either definite pictures as Alternating Hemiplegia of Childhood (AHC), Rapid-onset Dystonia-Parkinsonism (RDP) and CAPOS (cerebellar ataxia, areflexia, pes cavus, optic atrophy and sensorineural hearing loss), or a number of intermediate phenotypes, also presenting with epilepsy, neurodevelopmental delay, ataxia, oculomotor abnormalities and movement disorders [1,2]. Since curative and target-specific treatments are still lacking, therapeutic efforts

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usually point at symptomatic relief or at preventing the reoccurrence of paroxysmal phenomena [1]. At this purpose flunarizine showed significant effectiveness in numerous patients with AHC [3] and in one case of RDP [4]. Overall, beside antiepileptics (AEDs) for seizures control [1,3] very few alternative treatments have been approached in patients with ATP1A3-related diseases.

Aimed at expanding the knowledge on therapeutic opportunities for ATP1A3 diseases, here we describe a case of ATP1A3-related early onset drug-resistant epileptic encephalopathy responsive to ketogenic diet (KD).

2. Case report

The patient was a boy, born at the 36th week of Caesarean birth for oligohydramnios. First months of life were regular. Since the third month, he presented arrest of motor development and clonic seizures on the right side associated with sporadic episodes of hyperpnoea. The child also exhibited scarce spontaneous motility with marked axial hypotonia, poor visual contact and occasional horizontal nystagmus. After brain images and metabolic tests, resulted both normal, and EEG, showing spikes and slow waves in left fronto-temporal region, patient started an antiepileptic treatment. Seizures were

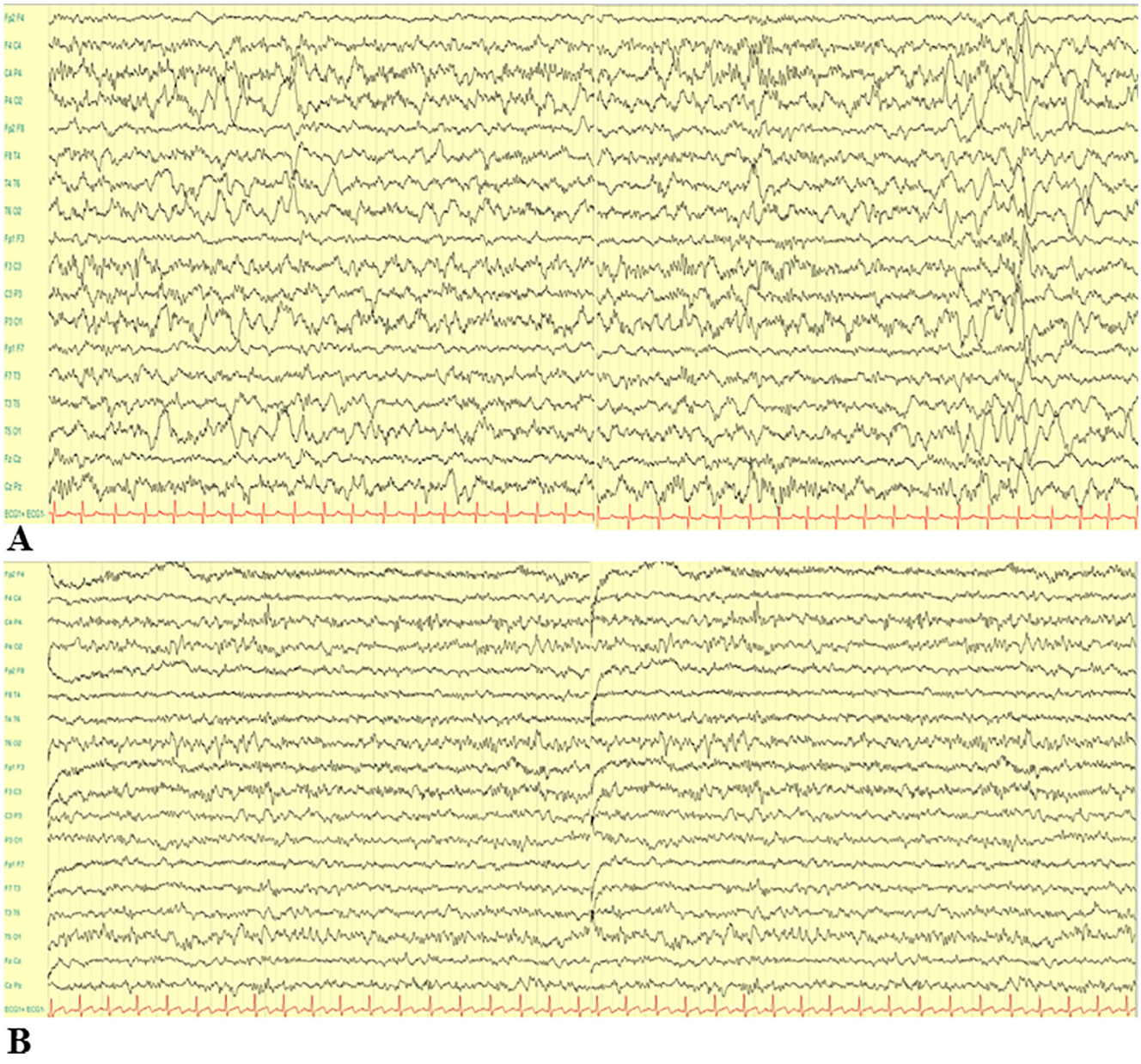

Fig. 1. A: Exemplary screenshots of EEGs before ketogenic diet showed bilateral delta slow waves in temporal region and poor organization and differentiation of the background rhythm. B: exemplary screenshots of EEGs after several months from the beginning of the ketogenic diet. A background rhythm activity was more differentiated and organized, no abnormal activity was recorded.

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