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Case Report

Coenzyme Q10 deficiency due to a COQ4 gene defect causes childhood-onset spinocerebellar ataxia and stroke-like episodes

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ABSTRACT

Primary coenzyme Q10 deficiency-7 is caused by homozygous or compound heterozygous mutations in the COQ4 gene. Until now 12 patients have been reported, most presenting with a lethal infantile phenotype with encephalopathy, epilepsy and cardiomyopathy. We report on a new phenotype of COQ4 deficiency: a childhood onset spinocerebellar ataxia with stroke-like episodes.

List of abbreviations

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1. Introduction

Coenzyme Q10 (ubiquinone; CoQ10, EC 206-147-9) is essential for mitochondrial respiratory chain electron transport [1,2]. Primary CoQ10 deficiency is caused by mutations in genes of the COQ10 biosynthetic pathway. Primary coenzyme Q10 deficiency-7 (COQ10D7, MIM 612898) is caused by homozygous or compound heterozygous mutation in the COQ4 gene (MIM 612898). Symptoms include early onset encephalomyopathy, cerebellar ataxia and nephropathy [3]. A first patient with CoQ10 deficiency due to COQ4 haploinsufficiency was published in 2012 [4]. So far a total of 12 patients with compound heterozygous or homozygous COQ4 variants have been reported, most (11/12) patients presented with a lethal infantile phenotype with encephalopathy, epilepsy and cardiomyopathy [5–7]. We report on a new phenotype of COQ4 deficiency: a childhood onset spinocerebellar ataxia with stroke-like episodes.

2. Patients and methods

The family pedigree is shown in Fig. 1: V-3 is patient 1 and V-4 is patient 2. Patient V-3 and V-4 have four healthy siblings and one younger brother with a complex constellation of congenital abnormalities not caused by mutations in the COQ4 gene.

Patient 1 is the 15 year old third child of consanguineous parents. His early psychomotor development was abnormal with delayed speech development. He developed a "tremor" at the age of four years. Physical examination was otherwise unremarkable. There were no dysmorphic features, no skin abnormalities and no hepatosplenomegaly. Brain MRI at age 5 revealed a suspected tectal glioma. He was treated with radiotherapy and the lesion has been stable since age 10. However, ambulation progressively deteriorated, and he became wheelchair dependent around age 12. On neurological examination there was dysarthria, spastic tetraparesis and prominent ataxia of upper and lower...
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References