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Mitochondrial cardioencephalopathy due to a COQ4 mutation

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Letter to the Editor

We read with interest the article by Sondheimer et al. about an infant male with mitochondrial cardio-encephalopathy and CoQ10 deficiency due to a COQ4 mutation [1]. We have the following comments and concerns.

The newborn obviously had developed mitochondrial multiorgan disorder syndrome (MIMODS), manifesting in the brain (hypotonia, seizures, microcephaly, cortical T1-hyperintensities, cerebral lactic elevation), the ears (hypoacusis), the myocardium (cardiomyopathy), and the intestines (gastro-esophageal reflux) (Table 1) [2]. Was the patient also screened for involvement of the endocrine organs, the bone marrow, the skin, and the lungs, also frequently involved in MIMODS?

How to interpret the cortical T1-hyperintensities? Was it due to bleeding, ischemia, inflammation, or due to the metabolic break-down? Was it the morphological equivalent of the seizures? Did it disappear after sufficient seizure control? Did the patient undergo lumbar puncture and cerebrospinal (CSF) investigations? Was there any indication for elevated lactate, pleocytosis, or an immunological reaction to the metabolic defect in the CSF?

Nothing is reported about treatment with conezyme-Q (ubiquinone), which has been previously reported to be highly effective in single cases with coenzyme-Q deficiency [3]. Coenzyme-Q may be even effective in mitochondrial epilepsy [4]. Did the patient receive coenzyme-Q and in which dosage? Was any beneficial effect observed?

The patient developed epilepsy since day 7 after birth, being treated with phenobarbital, topiramate, and clobazam [1]. From phenobarbital it is well known that it can be mitochondrion-toxic [5]. Did the authors consider that deterioration of the clinical manifestations could have resulted from application of this antiepileptic drug?

We should be more comprehensively informed about the family history. Was the mutation assessed as de novo or inherited? Were any other first-

Table 1
Manifestations of *COQ4* mutations.

Organ	Manifestation	Reference
Cerebrum	Epilepsy	[1, Chung 2015, Brea-Calvo 2015]
	Central hypotonia	[1, Chung 2015, Brea-Calvo 2015]
	Cerebellar atrophy	[Chung 2015, Brea-Calvo 2015]
	Mental retardation	[Salviati 2012]*
	Brainstem hypoplasia	[Chung 2015]
	Microcephaly	[1]
Heart	Cardiomyopathy	[1, Chung 2015]
	Arrhythmia	[1, Brea-Calvo 2015]
	Heart failure	[Brea-Calvo 2015]
Intestines	Reflux	[1]
Other	Lactic acidosis	[1, Chung 2015]
	Dysmorphism	[Salviati 2012]*

The case described by Salviati et al. also carried a deletion of chromosome 9q34.13.

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degree family members affected? Did any of them carry the mutation of the index case? Were the parents consanguineous?

Overall, this interesting case requires supplementary clinical and genetic investigations.

There are no conflicts of interest.

Both authors contributed equally.

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