Molecular Genetics and Metabolism Reports 10 (2017) 100

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism Reports

journal homepage: www.elsevier.com/locate/ymgmr

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Low blood heteroplasmy-rate may cause late-onset MELAS☆,☆☆,★

Keywords:
Mitochondrial
Cardiomyopathy
Myopathy
Cardiac involvement
Heart failure
Sudden cardiac death

Letter to the Editor

The interesting article by Sunde et al. about a 54 yo female with MELAS due to the m.3243A>G mutation with a blood heteroplasmy-rate of 31% and manifesting with recurrent stroke-like episodes(SLEs), tonic-clonic seizures, migraine, hypothyroidism, short stature, fatigability, and hearing-loss [1] raises the following comments and concerns.

For epilepsy the patient was initially treated with levetirazetam, phenytoin, and lamotrigine [1]. Which was the daily dosage of each of these antiepileptic drugs(AEDs)? Why were three AEDs applied for prophylaxis? Which were the serum levels of these AEDs? From phenytoin it is well-known that it is mitochondrion-toxic [2]. Why was it nonetheless given? Did seizures occur shortly before, during, or long after a SLE? Was confusion after starting AEDs attributable to phenytoin? Clonazapan is no AED. Do the authors mean clonazepam?

A heteroplasmy-rate of 31% in lymphocytes is low. Was heteroplasmy-rate determined also in other tissues, such as hair follicles, buccal mucosa, urinary epithelial cells, or muscle? Were heteroplasmy-rates higher in other tissues? Heteroplasmy-rates are reported to increase over time in post-mitotic tissues [3]. Were heteroplasmy-rates repeatedly determined during the disease course? Did they indeed increase over time?

SLEs typically go along with a stroke-like lesion on cerebral MRI(cMRI) [4]. Did the patient ever undergo a cMRI during a SLE? Was a characteristic vasogenic edema not concurring within a vascular territory seen in the acute stage?

Up to 25% of the mtDNA point mutations are sporadic with a family history negative for the disease [5]. Did the mother of the patient carry the mutation? Was hearing impairment the only clinical manifestation of MELAS in the mother? Which was the heteroplasmy-rate in the mother?

Overall, this interesting case could profit from discontinuation of phenytoin, from cMRI studies during a SLE, from genetic studies of the mother and her offspring, and from determination of the heteroplasmy-rates in tissues other than lymphocytes.

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18 January 2017

☆ There are no conflicts of interest
☆☆ No funding was received
★ Author contribution: JF: design, literature search, discussion, first draft, SZ-M: literature search, discussion, critical comments

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http://dx.doi.org/10.1016/j.ymgmr.2017.01.010