Onset of MELAS due to the m.3243A > G mutation is early if the large phenotypic variability is considered

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Letter to the Editor

With interest we read the article by Sunde et al. about a female with MELAS syndrome with onset at age 49 years and four stroke-like episodes (SLEs) during the first 2 years who was followed-up for 5 years [1]. We have the following comments and concerns.

The morphological equivalent of a SLE is a stroke-like lesion on cerebral MRI during the acute stage. Only one MRI during the asymptomatic stage is described showing left occipital cystic encephalomalacia and white matter lesions [1]. No MRI figure is presented. The patient is reported to have had experienced four SLEs during the first 2 years after diagnosis [1]. Were ever typical abnormalities (DWI and ADC hyperintensity beyond a vascular territory) detected in the acute stage during any of these SLEs? Did these lesions change in a typical manner over time [2]? How did the authors exclude that the occipital lesion resulted from an ischemic stroke?

We do not agree with the notion that MELAS was of late onset [1]. The patient is of short stature since childhood, hypothyroidism was detected at age 30 years, and hypoacusis started in her mid-30s [1]. Additionally, the patient had migraine, most likely since adolescence, and nausea. These are all typical manifestations of the m.3243A>G mutation, why physicians could have suspected a mitochondrial disorder (MID) much earlier [3]. When did nausea and migraine start?

A mainstay of treating MIDs is the avoidance of mitochondrion-toxic drugs [4]. Why did the patient receive phenytoin, of which it is well-known that it has mitochondrion-toxic properties and should be avoided in MIDs [4]. Why does she require four antiepileptic drugs (AEDs)? Was ever a monotherapy with increased lamotrigine tried? The patient complains about generalised fatigue during follow-up [1]. Is levetiracetam or clonazepam the culprit?

Overall, SLEs require MRI documentation, the patient might profit from modification of her AED-therapy, and all phenotypic manifestations should be considered when diagnosing MELAS.

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