MELAS can be psychiatric and neurological

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eNeurologicalSci 11 (2018) 3–4

Contents lists available at ScienceDirect

eNeurologicalSci

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

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ARTICLE INFO

Keywords:
Mitochondrial
mtDNA
Phenotype
Genotype
MELAS
Stroke-like episode
Epilepsy

Letter to the Editor

We read with interest the article by Ge et al. about a 37 years old female with MELAS syndrome due to the m.3243A > G variant, manifesting with short stature, hearing impairment, psychiatric disease (agitation, acoustic hallucinations), hypothyroidism, apraxia, alexia, epilepsy, migraine, arterial hypotension, lactic acidosis, and a stroke-like episode (SLE) [1]. We have the following comments and concerns.

We should be informed which of the clinical abnormalities were transient and attributable to the SLE and which remained part of the long-term phenotype. It is conceivable that manifestations of the SLE included seizures, the psychiatric abnormalities, apraxia, and alexia. Additional features, which may be attributable to a SLE include hemianopia, muscle weakness, aphasia, cognitive impairment, and psychosis [2]. Which of these additional features were present in the presented patient? We would also like to know if SLE manifestations completely resolved and after which time the status quo ante was reached. Occasionally, different SLEs overlap or follow consecutively each other [3].

It is reported that the SLE showed up on MRI as hyperintensity on DWI and as hypointensity on ADC, thus suggesting a cytotoxic edema. Cytotoxic edema is characteristic for ischemic stroke. Thus, we should be informed by which means an ischemic stroke was excluded in the presented case. Which was the cardiovascular risk profile of this patient? MELAS may be also associated with cardiac disease, including systolic dysfunction and atrial fibrillation, diabetes, and hyperlipidemia [4,5]. Did the patient present with atrial fibrillation, systolic dysfunction, noncompaction, diabetes, nicotine smoking, or hyperlipidaemia? Were carotid ultrasound or angiography of the extra-cerebral arteries normal?

Cerebro-spinal fluid (CSF) investigations were normal but it is not mentioned if CSF lactate was determined [1]. According to the MR-spectroscopy there was lactate elevation in the CSF [1]. Was CSF lactic acidosis confirmed by direct determination of the lactate in the CSF?

Did the patient receive L-arginine orally or intravenously and which dosage was applied during the acute respectively chronic stage of the SLE? Particularly during the acute stage of the SLE intravenous L-arginine should be applied, unless there are any contraindications against administering this agent.

Obviously, the patient received phenobarbital as an antiepileptic drug without detailing the dosage and the duration of the application [1]. From phenobarbital it is well known that it is mitochondrion-toxic [6]. Did the phenotype deteriorate after administration of phenobarbital? Were also other antiepileptic drugs applied?

We do not agree with the statement that thyroid dysfunction is rare in MELAS/MIDs. Thyroid dysfunction is one of the dominant clinical manifestations of MELAS [7] and frequently not attributed the underlying metabolic disease. However, endocrine disease in general is a prominent phenotypic feature of MELAS and mitochondrial disorders in general, why presence of thyroid dysfunction should always raise the suspicion of an underlying mitochondrial defect.

mtDNA mutations are usually present in the heteroplasmic form in mitochondrial disorders. Which were the heteroplasmy rates in blood and parenchymatous organs, such as liver, kidneys, or the myocardium. Was there a difference between the heteroplasmy rates of the saliva, fibroblasts, muscle, blood lymphocytes, or the urothelial cells?

mtDNA mutations are maternally transmitted in two thirds of the cases [8]. We should be informed if the patient's family history was positive for a mitochondrial defect in first-degree relatives, and if the mutation was also found in other clinically or subclinically affected members of the family?

Overall, this interesting case could be more meaningful if the family history would have been provided, if genetic studies would have been extended to first-degree family members, if heteroplasmy rates of the m.3243A > G variant would have been provided in various tissues, if the multisystem natures of MELAS would have been addressed, and if organs/tissues not obviously affected, would have been investigated prospectively.

Conflicts of interest

There are no conflicts of interest.

Funding

No funding was received.

https://doi.org/10.1016/j.ensci.2018.04.002
Received 22 December 2017; Accepted 10 April 2018
Available online 13 April 2018

Author contribution

JF: design, literature search, discussion, first draft, SZ-M: literature search, discussion, critical comments.

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