Mitochondrial Myopathy, Encephalopathy, Lactic Acidosis, and Stroke-like Episodes (MELAS) due to a m.10158T>C ND3 Mutation with a Normal Muscle Biopsy

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【 LETTERS TO THE EDITOR 】

Mitochondrial Myopathy, Encephalopathy, Lactic Acidosis, and Stroke-like Episodes (MELAS) due to a m.10158T>C ND3 Mutation with a Normal Muscle Biopsy

Key words: muscle biopsy, mitochondrial, mtDNA, respiratory chain, genetics

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To the Editor We read with interest the article by Mukai et al. regarding a 41-year-old male with mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome due to the mtDNA mutation m.10158T>C in the MT-ND3 gene with a heteroplasmy rate of 69% in the muscle (1). Our comments and concerns regarding this manuscript are described below.

The patient underwent a muscle biopsy, but no biochemical investigations were reported (1). Since a ND3 mutation was found, we can expect deficiency at least in complex-I of the respiratory chain. What were the results of the biochemical investigations of the muscle homogenate?

Seizures are frequent phenotypic manifestations of MELAS syndrome- particularly in association with stroke-like-episodes. Interestingly, the patient received a combination of three antiepileptic drugs (AEDs): levetiracetam (1,000 mg/d), zonisamide (400 mg/d), and carbamazepine (400 mg/d). Why was the dose of levetirazetam or zonisamide not further increased? Why was carbamazepine added despite being known to be mitochondrion-toxic, risking further enhancement of the seizure activity (2)? It is also well-established that a ketogenic diet may have antiepileptic properties with a beneficial effect on seizure frequency in patients with mitochondrial epilepsy (3). Was the patient put on a ketogenic diet and was it effective, possibly avoiding the patient to require AEDs? Was carbamazepine the cause of further deterioration of the patient's cognitive function?

The heteroplasmy rates of mtDNA mutations vary considerably between different tissues (4). Were heteroplasmy rates also determined in buccal cells, hair follicles, blood lymphocytes, fibroblasts, or urinary epithelial cells? Were heteroplasmy rates in these tissues different from those in the skeletal muscle? How do the authors explain that the heteroplasmy rate of the mutation was 69% in muscle tissue despite the fact that the muscle was neither clinically nor histopathologically affected? Which method was used to determine the heteroplasmy rate in the muscle?

The authors report that the family history was negative for clinical manifestations of a mitochondrial disorder (MID) (1). However, we should nevertheless be informed about any previous diseases or health problems in all first-degree relatives, including those usually not related to a MID. Any health problem affecting a relative must be considered, since any tissue can be affected by a mitochondrial defect.

MIDs frequently manifest phenotypically in the heart with hypertrophic or dilative cardiomyopathy, non-compaction, conduction disturbances, arrhythmias, or pulmonary hypertension (5). Were both patients screened for cardiac disease or was cardiac disease found in any of the first-degree relatives? Occasionally, abnormalities are found only when actively searched for.

Overall, this interesting case may profit from more extensive investigations of the muscle biopsy, an extensive family history, a thorough cardiological investigation, and an explanation of the inconsistencies described above.

The authors state that they have no Conflict of Interest (COI).

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