Letters to the Editor

Rhabdomyolysis in MELAS may be multifactorial

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With interest we read the article by Yokoyama et al. about a 24yo male with MELAS syndrome due to the tRNA(Lys) mutation m.3243A>G who developed a status epilepticus after alcohol consumption in the absence of a stroke-like episode (SLE)[1)]. We have the following comments and concerns.

Since some of the antiepileptic drugs (AEDs), in particular valproic acid, carbamazepine, phenobarbital, and phenytoin are mitochondrion-toxic, it is important to know which AEDs were applied for the status epilepticus, in which dosage, and for how long.

Rhabdomyolysis may have various etiologies[2)]. Rhabdomyolysis in the presented patient was most likely a complication of the status epilepticus. Were alternative causes of rhabdomyolysis, such as alcohol intoxication or drugs other than the AEDs, considered?

Was quadriparesis attributed to rhabdomyolysis or did the patient also manifest with myopathy as could be suspected from the muscle biopsy[1)]? Did quadriparesis resolve after resolution of rhabdomyolysis?

It is well known that seizures in MELAS are not exclusively related to SLEs. Seizures unrelated to a SLE may even trigger a SLE, why it is recommended to carry out follow-up cerebral imaging after a seizure in MELAS patients. When was the last cerebral MRI carried out after the status epilepticus in the presented patient?

A heteroplasmy rate of 20% in lymphocytes does not explain the presented phenotype. Was the heteroplasmy rate also determined in hair follicles, urine bladder epithelium, skin fibroblasts, buccal cells, or the muscle? Were heteroplasmy rates different between these tissues?

The family history was positive for diabetes (mother) and depression (mother, brother)[1)]. Was the m.3243A>G mutation also detected in these two relatives?

Was the patient investigated for follow-up? Did he experience further seizures after the status epilepticus? Did he tolerate the levetiracetam dosage on the long run?

Stroke-like lesions, the morphological equivalent of a SLE, are characterised by DWI hyperintensity and high signal on ADC in the acute stage, indicating a vasogenic edema[3)]. Extension of the lesion does not concur with any vascular territory. Occasionally, areas of a cytotoxic edema can be detected within a stroke-like lesion[4)]. Some MELAS patients may also manifest phenotypically with arrhythmias, conduction defects, cardiomyopathy, diabetes, mitochondrial hyperlipidemia, or mitochondrial hypertension, why they occasionally experience an ischemic stroke from atherothrombosis or cardioembolism. Which were the cardiovascular risk factors in this patient?

Concerning the treatment of MELAS and epilepsy it would be interesting to know if the patient was put a ketogenic diet or if he received NO-precursors during or after the status epilepticus.

We do not agree that growth of the patient was normal. At age 24yo he was 162 cm tall and according to the Austrian reference limits he was of short stature, a frequent manifestation in MELAS[5)].

Overall, this interesting case requires follow-up investigations and a family screening for MELAS. We also should be informed about heteroplasmy rates in tissues other than lymphocytes to explain the discrepancy between the low heteroplasmy rate and the severe clinical presentation.

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