Letter to the editor

Cerebellar stroke-like lesions in Leigh syndrome due to the variant m.8993T > C in MT-ATP6

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Letter to the Editor

With interest we read the article by de Veiga et al. about an 8 years old male with Leigh syndrome due to the mtDNA variant m.8993T > C in the MT-ATP6 gene [1]. The heteroplasmy rate of the variant was 98% in the muscle [1]. We have the following comments and concerns.

We do not agree that the cerebellar lesions were attributable to primary or secondary micro-angiopathy [1]. The patient had no evidence for the presence of risk factors for secondary micro-angiopathy, such as arterial hypertension, hyperlipidemia, diabetes, or smoking. Magnetic resonance angiography (MRA) was normal. Though primary (genetic) micro-angiopathy may be a phenotypic feature of mitochondrial disorder (MIDs) in general [2], there is no evidence in the index patient for migraine-like headache or peripheral retinopathy being interpreted as manifestations of primary micro-angiopathy [2]. The only indications for primary micro-angiopathy in the described patient are the white matter lesions (WMLs), but they can be due to other causes as well. To proof the suspicion of primary or secondary micro-angiopathy it is crucial that histological studies were carried out. A further argument against micro-angiopathy is that microbleeds may not only result from micro-angiopathy but may result from necrosis or coagulation disorders as well.

Recently, stroke-like lesions (SLLs), the morphological equivalent of a stroke-like episode (SLE), have been reported in the cerebellum [3]. Since the pathogenesis of the cerebellar lesion in the index patient is unclear and since fig. 1 (panels G, H) do not convincingly demonstrate an ischemic stroke, a cerebellar SLL should be considered. SLLs are not confined to a vascular territory and in the acute, expanding stage characterised by hyperintensity on diffusion weighted imaging (DWI), hyperintensity on apparent diffusion coefficient (ADC) maps, hyperperfusion on perfused weighted imaging (PWI) or perfusion single photon emission computed tomography (SPECT) and reduced oxygen extraction on oxygen extraction fraction (OEF) MRI [4]. Thus, we should be informed if there was hyperperfusion on PWI or perfusion SPECT at the initial investigation and if ever an OEF-MRI was carried out to document reduced oxygen extraction from cerebral blood.

We also do not agree that basal ganglia/thalamic lesions in Leigh syndrome, which are isointense on DWI/ADC but hyperintens on T2/FLAIR. There are also basal ganglia/thalamic lesions, which are hyperintens on DWI and ADC, thus indicating a vasogenic edema.

Missing is the report of the findings of electroencephalography (EEG). Since SLEs are assumed to be triggered by epileptiform activity [5], we should know if epileptiform activity was ever observed or recorded on EEG.

The patient is described with muscle wasting at the initial investigation [1]. We should be informed if muscle wasting was due to inactivity, myopathy, neuropathy, or neuronopathy. To clarify the cause of muscle wasting we should know the results of nerve conduction studies, needle electromyography, and muscle biopsy. Did the patient undergo MRI of the skeletal muscles? Particularly the results of the muscle biopsy would be interesting with regard to immune-histology, electron microscopy, and biochemical investigations of respiratory chain functions. In the light of the high heteroplasmy rate in the muscle, muscle wasting was most likely due to myopathy.

A further shortcoming of the study is that the current medication the patient was regularly taking was not provided.

Taken together, the reported study could profit from discussing the cerebellar lesion as SLL and from presentation of results of PWI, SPECT, OEF-MRI, EEG, nerve conduction studies, and electromyography. Muscle wasting needs to be explained and the influence of the current medication the patient was regularly taking on the condition needs to be discussed.

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Author contribution

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

Declaration of Competing Interest

There are no conflicts of interest.
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