Optimising therapeutic strategies for acute stroke-like lesions in MELAS

Letter to the Editor

With interest we read the article by González-Pinto González et al. about the management of a first ever stroke-like episode (SLE), with a corresponding stroke-like lesion (SLL), which was hyperintense on fluid attenuation inversion recovery (FLAIR) and diffusion weighted imaging (DWI) but isointense on apparent diffusion coefficient (ADC) maps, in a 38 years old male, who was diagnosed with mitochondrial encephalopathy, lactic acidosis, and stroke-like episode (MELAS) syndrome at age 30 years upon the clinical presentation (hypoacusis, permanent hypercreatine-kinase (CK)-emia), a positive family history for MELAS (maternal uncle), and the detection of the variant m.3243A > G [1]. The SLE occurred despite regular intake of L-carnitine, coenzyme-Q (CoQ), and L-arginine (21 g/d) starting at age 30 years [1].

Quite unusual is that cerebro-spinal fluid (CSF) investigations were normal in the index case. Since the patient was admitted with at least two SLLs, it can be expected that at least CSF lactate was elevated. Lactate elevation in the serum or CSF is pathognomonic for MELAS. Was the CSF investigated for lactate? We should know in this respect why magnetic resonance spectroscopy (MRS) did not show the expected lactate elevation at least within the two SLLs seen on cerebral computed tomography (CCT) and magnetic resonance imaging (MRI). How do the authors explain elevation of lactate in the serum but not the CSF?

Missing in this report is the heteroplasmy rate of the m.3243A > G variant in the index case. Severity of the phenotype is usually correlated with increasing heteroplasmy rates. We also should be informed in which tissue the variant was detected. Blood lymphocytes, muscle, urine epithelial cells, skin fibroblasts, or hair follicles cells? Missing is also the mtDNA copy number.

It is unclear if the patient was dismissed with an anti-seizure drug (ASD) therapy or not. We should know if levetiracetam (LEV) and lacosamide (LAC) were given only during the presence of the non-convulsive epileptic state or also after discontinuation of the seizure activity. We should know the maximal dosage of LEV and the maximal dosage of LAC, which was necessary to stop the epileptic state. We should know in this respect if the patient ever experienced a seizure after the SLE during follow-up.

The morphological outcome of a SLL can be quite heterogeneous [2]. A SLL may end up as white matter lesion (WML), focal atrophy, cyst, laminar cortical necrosis (LCN), or as toenail sign. There is also the possibility that no structural abnormality persists. How did the SLL look like on the last follow-up MRI?

SLLs in the acute stage not only present with hyperintensity on T2/FLAIR, DWI, and ADC, but also on perfusion weighted imaging (PWI). Additionally, the area of the SLL may be hypointense on oxygen extraction fraction (OEF)-MRI [3]. We should know if PWI and OEF modalities were applied and if the results were compatible with a SLL. Since the patient experienced recurrent CK-elevation, we should know if there were any indications for myopathy, such as weakness, wasting, cramping, easy fatigability, reduced tendon reflexes, a myogenic electromyography, or muscle biopsy findings indicative of a mitochondrial disorder.

We do not agree with the notion that the index patient is the first adult case with good clinical outcome after “quick implementation of this approach” [1]. Several adults receiving ASD in addition to NO-precursors have been reported which responded favourably under this regimen [4–6].

Overall, this interesting case report could profit from provision of additional data, such as heteroplasmy rates, MRI sequences, and details on the therapeutic management of the acute SLE. SLEs may respond to ASDs if there are seizures or epileptiform discharges on EEG, to NO-precursors, but also to antioxidants, co-factors, or the ketogenic diet. It should be stressed that supplementation of LEV by LAC may stop seizure-activity associated with a SLE.

Author contribution

JF: design, literature search, discussion, first draft,

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Declaration of Competing Interest

None.

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