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Letter to the Editor

Diagnostic and therapeutic aspects of Leigh syndrome due to the variant m.10197G > A

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Letter to the Editor,

With interest we read the article by Tolomeo et al. about three unrelated males aged 7y (patient 1), 5y (patient 2) and 4y (patient 3) respectively with Leigh syndrome due to the variant m.10197G > A in the *ND3* gene [1]. We have the following comments and concerns.

In patient 2 MRI at age 5y was described to show stroke-like lesions (SLLs) characterised by a mixed vasogenic and cytotoxic edema [1]. However, the morphological appearance is not convincing of SLLs. We should be informed if these lesions were hyper- or hypo-intense on ADC, if these lesions were accompanied by clinical manifestations suggestive of a stroke-like episode (SLE), if perfusion studies showed hyperperfusion [2], if epileptiform discharges were recorded on EEG [3], and if oxygen extraction was reduced in these areas, a typical feature of SLLs [4]. Due to the absence of a typical SLL in patient 2 we do not agree with the description of the phenotype in this patient as MELAS. The authors themselves describe the phenotype of all three patients in the abstract as Leigh syndrome.

The MRI of patient 2 showed mixed vasogenic and cytotoxic edema [1]. Thus, it would be interesting to know the cause of cytotoxic edema, particularly if there were any cerebrovascular risk factors, if the cytotoxic lesions were seizure-associated, or if there was vasospasm.

Left-sided hemiparesis in patient 3 was described as progressive. However, description of the MRI does not explain hemiparesis [1]. Which was the morphological equivalent of hemiparesis in this particular patient? Was hemiparesis do to a SLL, an ischemic stroke, a focal seizure, due to acute demyelinating encephalomyelitis (ADEM), or a brainstem lesion?

According to Figure 4A 9% of the m.10197G > A carriers develop seizures but in the main text it is mentioned that 20% of the m.10197G > A carriers develop seizures [1]. How do the authors explain this discrepancy?

Direct measurement of lactate in the CSF was normal in patient 1. However, elevated lactate can be documented by MR-spectroscopy (MRS) within the cerebral parenchyma. Thus, we should be informed if MRS was applied in patent 1 and if a lactate peak was visible.

Patient 2 obviously had cardiac involvement. Thus, the results of the long-term ECG recordings and the result of echocardiographic studies should be presented. It would be also helpful to know the values of creatine-kinase, troponin, and of proBNP in this patient. It should be also explained what the authors mean by mid-aortic syndrome.

Patients with Leigh syndrome frequently do not only manifest in the CNS but also in other organs, such as the ears, eyes, endocrine organs, the heart, or the kidneys. Thus, it would be helpful if the three patients were prospectively investigated for clinical or subclinical multiorgan involvement.

Patient 2 received a combination of three anti-epileptic drugs (AEDs). We should be informed about the seizure types, the seizure frequency, the dosages of the AEDs and for how long they were given. Since patients with mitochondrial epilepsy may also respond to a ketonic diet [5,6], we should be informed if this regimen was tried in patient 2 and if it was effective and saved dosage and number of AEDs.

SLEs can be treated with NO-precursors, AEDs, antioxidants like coenzyme-Q, edaravone, or idebenone, steroids, or a ketogenic diet. We should be informed which of these approaches was applied during the acute stage of the SLE in patient 2.

Overall, this interesting case series could be more meaningful if some inconsistencies would be clarified, if more information about the treatment was provided, and if multiorgan involvement was prospectively assessed.

Author contribution

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

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The author contributed equally.
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