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Letter to the Editor

Antiepileptics and NO-precursors may be beneficial for stroke-like episodes

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ABSTRACT

Pathogenesis and management of stroke-like episodes in mitochondrial disorders is under debate and no consensus has been reached thus far how this phenomenon should be managed. Frequently applied are nitric oxide (NO) precursors but a well-designed study confirming the effectiveness of such an approach is lacking. Administration of antiepileptic drugs can be meaningful if there is paroxysmal activity on EEG or if a patient presents with seizures. The case reported by Sakai et al. suggests that administration of antiepileptic drugs for a stroke-like episode may be beneficial even in the absence of seizures or paroxysmal EEG activity.

Letter to the Editor

With interest we read the article by Sakai et al. about a 53 years-old female with MELAS syndrome due to the variant m.3243A > G in the *tRNA/(Leu)* gene [1]. The patient was admitted for a first stroke-like episode (SLE), which did not resolve upon administration of L-arginine alone but only after addition of levetirazetam [1]. We have the following comments and concerns.

DWI hyperintensity associated with ADC hypointensity suggests cytotoxic edema, and thus ischemic stroke. Stroke-like lesions (SLLs), the morphological equivalent of SLEs, usually show up as DWI hyperintensity associated with ADC hyperintensity [2]. Since the patient had the cardiovascular risk factors diabetes and arterial hypertension, it needs to be excluded that the bilateral occipital lesions were ischemic in nature and due to microangiopathy. Since the patient also had cardiac involvement in the form of cardiomyopathy it is conceivable that she also experienced paroxysmal atrial fibrillation leading to cardioembolism. We need to be informed if atrial fibrillation was excluded by long-term recordings of the ECG, which type of cardiomyopathy was diagnosed, and if left ventricular hypertrabeculation, also known as non-compaction, was definitively excluded. Noncompaction is frequently associated with cardioembolism resulting from thrombus formation within the deep intertrabecular recessus of the myocardium [3]. Administration of heparin intravenously for ischemic stroke, as initially applied in the presented case, is no standardised therapy of ischemic stroke. Which is the evidence for the effectiveness of such a therapeutic approach?

Though administration of antiepileptic drugs is well appreciated in the therapeutic management of SLEs with seizure activity [4], it is surprising that levetirazetam was given. The authors should explain upon which rationale levetirazetam was given since the patient had neither paroxysmal activity on EEG nor did the SLE manifest with focal or generalised seizures. Furthermore, it cannot be excluded that regression of the SLLs on MRI has to be attributed to the natural course of the abnormality and has nothing to do with any of the therapies applied. Such a scenario has to be considered as antiepileptic drugs can be ineffective in mitochondrial epilepsy but also in SLEs.

The patient was obviously underweighted with 32 kg and a body height of 149 cm [1]. Was the low body weight attributable to a gastrointestinal abnormality, to a specific diet the patient was taking regularly, to a hormonal problem, or to the drugs she was regularly taking? Did the patient suffer from a depressive disorder? Since mitochondrial disorders are more frequently associated with neoplasias than healthy subjects [5], we should be informed if a malignoma was definitively excluded in this particular patient. Gastrointestinal involvement in MELAS that could explain the low body weight is well appreciated and includes vomiting [6], pseudoobstruction, poor appetite, gastroesophageal sphincter dysfunction, constipation, dysphagia, gastroparesis, diarrhoea, pancreatitis, or stenosis of the duodeno-jejunal junction [7]. Patients with a MID are frequently recommended to adhere to a ketogenic diet to avoid glucose intake and stimulation of the glycolytic pathway. We should be informed if the presented patient was under such a diet or any other dietary regimen that could explain the low body weight. Was reduced body weight simply due to growth hormone deficiency, a rare endocrine manifestation in MIDs [8]. Since the ketogenic diet may exhibit beneficial effects in MELAS in general [9] and in mitochondrial epilepsy in particular [10], we should be informed if the patient was put on such a regimen.

A shortcoming of the report is that no heteroplasmy rates were provided. Since heteroplasmy rates may strongly influence the severity of the phenotype, it is essential to know the mutation load in affected and unaffected tissues.

Overall, this interesting case requires a broader discussion of the MRI findings, an explanation why antiepileptics were given and why no ketogenic diet was recommended, and provision of heteroplasmy rates in hair follicles, buccal mucosa cells, skin fibroblasts, muscle cells, lymphocytes, and urinary epithelial cells.

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Conflicts of interest

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