Therapeutic management of stroke-like episodes varies from that of encephalitis

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Abstract

Introduction: Stroke-like episodes (SLEs) are typical cerebral manifestations of certain mitochondrial disorders (MIDs). They are characterised by a vasogenic edema in a non-vascular distribution.

Patients concerns: none

Diagnosis: SLEs show up on cerebral MRI as stroke-like lesions (SLLs), characterised by vasogenic edema in a non-vascular distribution. SLLs expand in the acute stage and regress during the chronic stage. They show hyperperfusion in the acute stage and hypoperfusion in the chronic stage.

Interventions: SLLs respond favorably to antiseizure drugs, to No-precursors, steroids, the ketogenic diet, and antioxidants.

Outcome: SLLs end up as normal tissue, white matter lesion, grey matter lesion, cyst, laminar cortical necrosis, or the toenail sign.

Conclusions: SLLs are a frequent manifestation of MIDs. They undergo dynamic changes in the acute and chronic stage. They need to be differentiated from ischemic stroke as they are differentially treated.

Abbreviations: AED = antiepileptic drug, CSF = cerebrospinal fluid, EEG = electroencephalography, MELAS = mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes, MID = mitochondrial disorder, mtDNA = mitochondrial DNA, SLE = stroke-like episode, VPA = valproic acid.

Keywords: heteroplasmy, MELAS, mtDNA, oxidative phosphorylation, stroke-like episode

1. Introduction

In a recent article, Liu et al. reported about a 12yo Chinese male with mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) due to the mitochondrial DNA (mtDNA) variant m.3243A>G, clinically manifesting with a stroke-like episode (SLE) presenting with somnolence, sensory aphasia, quiet speech, dysphagia, agraphia, inability to wear clothes, recurrent vomiting, gait disturbance, fever, and paroxysmal electroencephalography (EEG) activity. We have the following comments and concerns.

2. Diagnosis

SLEs are a hallmark of MELAS. They are easy to diagnose upon application of the MRI where they appear as stroke-like lesion (SLL). SLLs may be acute or chronic. Acute SLLs are characterised by progressive, expansion of cortical/subcortical lesion in a non-vascular distribution, which is T2-hyperintense, DWI hyperintense, ADC hyper- or hypointense, PWI hyperintense, and OEF-MRI hypointense. Chronic SLLs regress in size, show hypoperfusion, and DWI and ADC abnormalities normalise.

3. Intervention and outcome

We do not agree with the statement that the m.3243A>G variant is located in the 12S-rRNA gene, as mentioned in the abstract and the body of text. The m.3243A>G variant is located in the tRNA (Leu)/MT-TL1 gene.

MtDNA variants are usually heteroplasmic. Thus, we should be informed about heteroplasmic rates at least in blood lymphocytes and urinary epithelial cells. Testing of mtDNA in urinary epithelial cells is preferred over mtDNA in blood lymphocytes.

Absence of an mtDNA variant in the mother of a mitochondrial disorder (MID) patient is not unusual as only 75% of the cases are maternally transmitted. However, since heteroplasmic rates vary significantly between tissues, not only blood lymphocytes but also hair follicles, buccal mucosa cells, skin fibroblasts, and muscle should be investigated in the mother of the index case.

The m.3243A>G variant is usually associated with reduced activity of complex-I and normal activity of complex-IV. Thus, we should know the results of biochemical investigations of muscle homogenate, particularly in the light of elevated creatine-kinase (CK) in the index patient.

The presented figures are not convincing with regard to the presence of cerebral edema with mass effect. Thus, more slices...
and modalities of the magnetic resonance imaging (MRI) should be presented. Accordingly, it is unclear why the patient received acyclovir, ceftriaxone, and dexamethasone. Cerebrospinal fluid (CSF) investigations were normal without any indication for bacterial or viral meningitis / encephalitis. We should know if tests for viruses or bacteria were carried out and if they were informative or not. Since SLEs usually go along with lactic acidosis in the CSF, we should know if CSF lactate was elevated or not. This is of particular interest in the light of the elevated lactate peak on magnetic resonance spectroscopy.

Since the patient presented with epileptiform discharges on EEG, we should know which type of antiepileptic drug (AED) treatment the patient received and in which dosage. Knowing the type of AED treatment is crucial as some of the AEDs (eg, valproic acid, carbamazepine, phenytoin, phenobarbital, topiramate) are potentially mitochondrion-toxic.

Treatment of SLEs should include AEDs, NO-precursors, and antioxidants. Seizures or epileptiform discharges on EEG are frequent features of a SLE, as in the presented patient. Coenzyme Q and L-carnitine are thought to increase mitochondrial energy production and to slow disease progression. L-arginine, L-carnitine and L-citrulline have been shown in single cases to decrease the severity of SLE and to decrease the frequency of SLEs. There are ongoing trials for coenzyme-Q and idebenone. Which is the reason why the patient did not receive antioxidants or AEDs despite epileptiform discharges on EEG? Were there any contraindication? Did the patient ever develop seizures?

Since MIDs are usually progressive, we should know the results of follow-up investigations and if new features of a MID developed over time.

We should be informed why the patient was unable to wear clothes. Was this due to allergy, dysesthesia, or allodynia or do the authors mean dressing apraxia?

4. Conclusions

Overall, this interesting case could be more meaningful if the m.3243A>G variant was correctly attributed to MT-TL1, if the mother was more extensively investigated, if it was explained why acyclovir, ceftriaxone, and dexamethasone were applied for the SLE, and if L-arginine or another NO-precursor was given. The study would also profit from presentation of follow-up investigations and from an explanation why the patient was unable to wear clothes.

Author contributions

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

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