Consider Stroke-Like Episodes as a Differential of Juvenile Strokes In m.3243A>G Carriers

Abstract:

Keywords: MELAS, stroke, stroke-like episode, mtDNA, respiratory chain, mitochondrial.

LETTER TO THE EDITOR

With interest we read the article by Reed, E. M. et al., (2020) about a 25yo male who was diagnosed with ischemic stroke upon the clinical presentation (acute aphasia) and a cerebral computed tomography (left temporo-parietal subacute lesion) (Reed, E. M. et al., 2020). Additionally, his history was positive for diabetes, attention-deficit/hyperactivity disorder, and pervasive development disorder (Reed, E. M. et al., 2020). The patient was later diagnosed with mitochondrial encephalopathy, lactic acidosis, and stroke-like episode (MELAS) syndrome upon lactic acidosis, recurrent seizures, laminar cortical necrosis, and documentation of the m.3243A>G variant in MTTL1 (Reed, E. M. et al., 2020). Nine months after diagnosing MELAS the patient was found dead on the floor and the cause of death was attributed to ketoacidosis after forensic autopsy (Reed, E. M. et al., 2020). We have the following comments and concerns.

We do not agree with ketoacidosis as the cause of death in this patient. MELAS is a multisystem disease, affecting not only the brain and the spinal cord, but also the eyes, ears, vestibulum, endocrine organs, the gastrointestinal tract, and the heart. More rarely, the lungs, kidneys, bone marrow, skeleton, and the skin may be affected. Differential diagnoses that should be considered as a cause of death in addition to ketoacidosis include sudden unexplained death in epilepsy (SUDEP), Takotsubo syndrome (TTS), cardiac arrest, ventricular arrhythmias, drug side effects or drug interactions, and pulmonary embolism. High vitreous glucose and β-hydroxy-butyrate not necessarily imply derailed diabetes. These elevated parameters could also indicate extreme stress. We should know the last HbA1c value and the last antidiabetic medication prior to decease.

Since the patient had epilepsy, we should know the types of seizures, the seizure frequency, the EEG results, the anti-seizure drug (ASD) regimen, the adherence to ASD treatment, and the ASD effect. Since stroke-like episodes (SLEs) frequently go along with either seizures or epileptiform discharges on EEG (Finsterer, J. 2019), we should know the results of electroencephalography (EEG) during hospitalisation for the “ischemic” stroke. With regard to TTS we should know if post-mortem catecholamine levels were determined. TTS is characterised by a massive elevation of serum catecholamines (catecholamine storm) (Sethi, P., & Peiris, C. D. 2020). With regard to cardiac arrest and ventricular arrhythmias we should know if ECG, long-term ECG, and echocardiography prior to decease were normal and if the history was positive for palpitations, syncope, or heart failure. Was pulmonary embolism excluded on autopsy?

A shortcoming of the study is that the “stroke” was diagnosed only upon CCT but not upon multimodal cerebral MRI. Most likely the initial stroke was not ischemic in nature but a so called stroke-like episode (SLE), which is the hallmark of MELAS but may occur also in other MIDs (Finsterer, J., & Aliyev, R. 2020). The morphological equivalent of a SLE on cerebral MRI is the so called stroke-like lesion (SLL). A SLL is characterised by T2-, DWI-, PWI- hyperintensity, and hypointensity on oxygen-extraction fraction MRI, which is not confined to a vascular territory (Finsterer, J., & Aliyev, R. 2020). SLLs show a progressive course with regard to intensity and extension and end up as normal brain tissue, cysts,
white matter lesion, toenail sign, or laminar cortical necrosis (Finsterer, J. 2020). SLLs may recur in the same or other locations, supra- or infra-tentorially. A strong argument in favour of a SLL in the index patient is that the MRI two months after the event showed laminar cortical necrosis. We should know if the onset of aphasia was truly acute or subacute.

Missing is the medication the patient was regularly taking prior to decease. Missing are the post-mortem creatine-kinase and lactate values.

Overall, this interesting case could profit from a discussion about alternative causes of sudden death including SUDEP, TTS, ventricular arrhythmias, cardiac arrest, and pulmonary embolism. High vitreous glucose and β-hydroxy-butyrate not necessarily imply ketoacidosis from diabetes.

REFERENCES