Deterioration of the m.8993T>G Associated Phenotype after General Anesthesia

Abstract:
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LETTER TO THE EDITOR

With interest we read the article by Lopes, T. et al., (2018) about a 3 years old female infant with Leigh syndrome due to the variant m.8993T>G (heteroplasmy >90%), with disease onset at age 8 months with generalised hypotonia and psychomotor retardation (Lopes, T. et al., 2018). The condition deteriorated suddenly one day after performing a cerebral MRI under anesthesia when the patient developed hyporeactivity, aggravated hypotonia, exaggerated tendon reflexes, and cutaneous pallor (Lopes, T. et al., 2018). Subsequently a transient, self-limiting episode of apnea and cyanosis with somnolence and increased prostration occurred (Lopes, T. et al., 2018). Phenytoin was begun. Serum lactate and citrulline were elevated and the MRI showed T2-hyperintesities of the putamen bilaterally (Lopes, T. et al., 2018). She later developed ataxia, dystonia, and epilepsy and received phenobarbital (PB), levetiracetam (LEV), and a vitamin cocktail (Lopes, T. et al., 2018). We have the following comments and concerns.

Patients with a mitochondrial disorder (MID) may develop adverse reactions to drugs for general or local anesthesia or for muscle relaxation (Finsterer, J. et al., 2005; & Thomas, M. et al., 2015). Thus, we should be informed which drugs were applied for anesthesia prior to the MRI and if deterioration could be attributed to side effects of these agents. Deterioration of the phenotype after anesthesia was more likely due to side effects to the drugs used for anesthesia than to metabolic stress induced by the anesthetic procedure, an infection, vaccination, or fasting, as suspected by the authors. Generalised anesthesia is usually well tolerated by MID patients if mitochondrion-toxic agents are avoided.

The subsequent episode of apnea was obviously interpreted as epileptic seizure in the absence of epileptiform discharges on electroencephalography (EEG) as the patient received phenytoin (PHT) (Lopes, T. et al., 2018). From PHT it is well known that it can be mitochondrion toxic (Finsterer J. 2016), why it should not be applied as first line medication for mitochondrial epilepsy. We should know if PHT was replaced by PB and LEV because of side effects or because of inefficacy. Furthermore, the therapeutic range of PHT is narrow and the majority of patients has serum levels below or above the therapeutic range (Shaikh, A. S. et al., 2018). There are also concerns regarding the application of PB to patients with a MID (Finsterer J. 2016). A further option for the anti-seizure management of mitochondrial epilepsy is the ketogenic diet (KD) (Paleologou, E. et al., 2017).

Leigh syndrome may not only be associated with elevated lactate in the serum but also in the cerebrospinal fluid (CSF) (Yamada, K. et al., 2012). Thus, we should know if the patient was investigated for concentrations of CSF lactate or if MR-spectroscopy (MRS) was carried out to document an increased lactate peak. Deterioration of the clinical condition...
may be attributed to lactic acidosis, why we should know if serum/CSF lactate was determined prior to the deterioration and if serum/CSF lactate was normal before.

Since patients with Leigh syndrome may not only present with involvement of the basal ganglia but also with involvement of the cerebellum (Chourasia, N. et al., 2018), we should know if ataxia was rather attributed to a cerebellar than to a basal ganglia lesion. In this respect it would be interesting to know if the patient had dysarthria, tremor, dysmetria, or nystagmus.

Since the variant m.8993T>G was obviously inherited from the mother (heteroplasmy rate: 75%) we should know if the mother manifested clinically or subclinically or not.

Overall, this interesting report could be more meaningful by providing supplementary information and discussion of unsolved issues, such as the trigger of the initial deterioration, toxic effect of PHT and PB, cause of ataxia, and presence of elevated lactate in the CSF. The mother should undergo a detailed neurologic exam.

REFERENCES