Letter to the Editor

Mitochondrial disorders are prone to propofol infusion syndrome

Dear Editor

With interest, I read the article by Shimizu *et al*.[1] about a 24-year-old woman with mitochondrial encephalopathy, lactic acidosis, and stroke-like episode (MELAS) syndrome due to the variant m.3271T>C in *MT-TL1* who survived a propofol infusion syndrome (PRIS) developing after administration of propofol for intractable seizures. Initially, she was admitted for impaired consciousness, quadriparesis, and generalized myoclonic seizures, which became refractory to treatment with levetiracetam, perampanel, lacosamide, and clobazam.[1] The patient survived PRIS having been treated by discontinuation of propofol and continuous hemodiafiltration.[1] The study has a number of shortcomings and raises concerns.

The main shortcoming is that the patient received propofol despite having been previously diagnosed with MELAS. From MELAS and other mitochondrial disorders it is well appreciated that propofol can be harmful to these patients.[2] Knowing the diagnosis and the literature about the mitochondrion-toxic effect of propofol, the authors should have prevented the application of propofol for intractable myoclonic state. Alternative antiseizure drugs could have been thiopental or ketamine.[3] It also should have been considered to put the patient on a ketogenic diet (KD), since it has been previously shown that a ketogenic diet can be beneficial even in mitochondrial disorders with intractable status.[4]

A second shortcoming is that the cause for admission, a stroke-like episode due to bilateral parietotemporal stroke-like lesions, was not encountered as such. Stroke-like episodes frequently present with epilepsy, confusion, weakness, visual impairment, headache, and vomiting, and manifest on magnetic resonance imaging as a stroke-like lesion (SLL) as shown in figure 1 of the case report.[5] Although the cause of SLLs remains elusive, several hypotheses have been raised to explain the condition (metabolic, vascular, and epileptogenic hypothesis). Following these hypotheses, the treatment most widely applied to SLLs include nitric oxide precursors (L-arginine and L-citrulline) and antiseizure drugs. Although the patient received L-arginine, we should know if the indication was the SLL and if she received it intravenously. Strong arguments for SLLs are that the bilateral lesions were not confined to a vascular territory and that these areas showed hyperperfusion.[1]

A further shortcoming is that the heteroplasmy rates of the pathogenic variant were not provided. Knowing the heteroplasmy rate in various tissues is crucial as they may correlate with the severity of the phenotype and may determine the disease trajectory and thus the outcome of these patients. Additionally, knowing heteroplasmy rates is crucial for genetic counselling.

It remains unclear why the non-convulsive epileptic state stopped despite discontinuation of propofol. We should know if this is the spontaneous disease trajectory, if propofol had been effective, or if the SLL had resolved.

Missing are biochemical investigations of the muscle homogenate to see if the variant m.3271T>C decreased complex II and III activity, as does propofol.

Overall, this interesting case has a number of shortcomings that need to be addressed before interpreting the findings. The authors should provide heteroplasmy rates, an explanation for the application of propofol in a MELAS patient, why the SLLs were missed, and why seizures stopped despite discontinuation of propofol.

DISCLOSURE

Approval of the research protocol: N/A.
Informed consent: N/A.
Registry and the registration no. of the study/trial: N/A.
Animal studies: N/A.
Conflict of interest: None.

Josef Finsterer,
Krankenanstalt Rudolfstiftung, Messerli Institute, Vienna, Austria
E-mail: fifigs1@yahoo.de

REFERENCES

1 Shimizu J, Tabata T, Tsujita Y *et al*. Propofol infusion syndrome complicated with mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes: a case report. Acute Med. Surg. 2019; 7: e473.
2 Mtaweh H, Bayır H, Kochanek PM, Bell MJ. Effect of a single dose of propofol and lack of dextrose administration in a child with mitochondrial disease: a case report. J. Child Neurol. 2014; 29: NP40–6.
3 Prüss H, Holtkamp M. Ketamine successfully terminates malignant status epilepticus. Epilepsy Res. 2008; 82: 219–22.

4 Sort R, Born AP, Pedersen KN, Fonsmark L, Uldall P. Ketogenic diet in 3 cases of childhood refractory status epilepticus. Eur. J. Paediatr. Neurol. 2013; 17: 531–6.

5 Finsterer J. Mitochondrial metabolic stroke: Phenotype and genetics of stroke-like episodes. J. Neurol. Sci. 2019; 400: 135–41.