Letter to the Editor



Valproate Is Contraindicated in POLG1 Mutations

Josef Finsterer

Neurological department, Krankenanstalt Rudolfstiftung, Vienna, Austria

To the Editor:

We read with interest the article by Park et al. [1] about a 10-month male subject with Alpers-Huttenlocher disease (AHD) due to the POLG1 mutations p.Arg807His and p. Arg627Trp, who was admitted for acute liver failure, underwent liver transplantation, developed intractable epilepsy, received valproate, and survived after discontinuation of valproate. We have the following comments and concerns regarding the content of the article.

When was valproate started and which dosages were applied? Which were the other five anti-epileptic drugs (AEDs) the patient received during hospitalization? AEDs can be mitochondrion-toxic, in particular, valproic acid, phenobarbital, carbamazepine, and phenytoin [2]. Was deterioration of the phenotype attributable to one or a combination of these AEDs? There was lactic acidosis on admission, suggesting mitochondrial disorder (MID) [1]. Why was valproate not discontinued at the time of suspicion of MID?

What was the cause of acute liver failure in the described patient? Was liver failure attributable to the current medication on admission? Which type of antibiotics did the patient receive for bronchitis? Was liver failure attributable to the underlying MID? Did

liver parameters remain elevated after liver transplantation, suggesting that they were rather the result of the medication applied than the underlying MID?

We do not agree with the statement that transplantation should be considered as an alternative option for treating patients with AHD [1]. Disadvantages of transplantation, in general, are that patients require long-term immunosuppression, surgery requires long duration of anesthesia administration, AHD patients usually survive for a short-term, MIDs may manifest in the immune system and may go along with primary immunosuppression [3], steroids may exhibit detrimental effects in MIDs [4], and the long-term outcome of patients with AHD may not improve with transplantation. Which type of immunosuppression was given to the patient? Which was the long-term outcome of the index case?

The patient was obviously compounded heterozygous for two POLG1 mutations [1]. Thus, it is conceivable that he received one mutation from the father and one from the mother. POLG1 mutations frequently cause depletion or multiple deletions of mitochondrial DNA (mtDNA) [5]. What was the rate of mtDNA depletion in this patient or were there any multiple mtDNA deletions?

Received: January 9, 2018, Revised: March 28, 2018, Accepted: April 6, 2018

Corresponding author: Josef Finsterer, Neurological department, Krankenanstalt Rudolfstiftung, Juchgasse 25, Vienna 1030, Austria. Tel: +43-171165, Fax: +43-14781711, E-mail: fipaps@yahoo.de

Copyright © 2019 by The Korean Society of Pediatric Gastroenterology, Hepatology and Nutrition
This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

What was the cause of multifocal hyperintensities on diffusion-weighted imaging? Was it attributable to a cytotoxic edema or a vasogenic edema? Was it hypo- or hyperintense on apparent diffusion coefficient? Were these lesions compatible with multiple embolic ischemic strokes, an epiphenomenon attributable to the seizures, or multifocal stroke-like episodes? Did these lesions resolve during follow-up? In case these lesions were interpreted as stroke-like lesions, did the patient benefit from L-arginine?

Overall, this interesting case report could be more meaningful if more clinical data would have been provided, particularly about the medication at the time of admission, during the 1-year long hospitalization, and during follow-up. It is also essential that the parents should have been clinically and genet-

ically investigated.

REFERENCES

- Park S, Kang HC, Lee JS, Park YN, Kim S, Koh H. Alpers-Huttenlocher syndrome first presented with hepatic failure: can liver transplantation be considered as treatment option? Pediatr Gastroenterol Hepatol Nutr 2017;20:259-62.
- 2. Finsterer J. Toxicity of antiepileptic drugs to mitochondria. Handb Exp Pharmacol 2017;240:473-88.
- 3. McKee DH, Cooper PN, Denning DW. Invasive aspergillosis in a patient with MELAS syndrome. J Neurol Neurosurg Psychiatry 2000;68:765-7.
- 4. Finsterer J, Frank M. Glucocorticoids for mitochondrial disorders. Singapore Med J 2015;56:122-3.
- Finsterer J, Ahting U. Mitochondrial depletion syndromes in children and adults. Can J Neurol Sci 2013; 40:635-44.