

Letter to the Editor

Management of epilepsy in Leigh-like syndrome due to the variant m.10191T>C in ND3

Finsterer J, MD, PhD*

¹Krankenanstalt Rudolfstiftung, Messerli Institute, Vienna, Austria

Article History

Received: 28.01.2020

Accepted: 10.02.2020

Published: 24.02.2020

Keywords: Leigh syndrome, heteroplasmy, complex-I defect, epilepsy, mtDNA, oxidative phosphorylation, anti-seizure drugs.

Journal homepage:

<https://www.easpublisher.com/easjms>

Quick Response Code



Copyright © 2020: This is an open-access article distributed under the terms of the Creative Commons Attribution license which permits unrestricted use, distribution, and reproduction in any medium for non commercial use (NonCommercial, or CC-BY-NC) provided the original author and source are credited.

With interest we read the article by Li *et al.*, about a 24 years old Chinese female with Leigh-like syndrome (LLS) due to the heteroplasmic mtDNA variant m.10191T>C in ND3 (Li, T. R. *et al.*, 2019). Manifestations at onset at age 18 years were seizures (Li, T. R. *et al.*, 2019). We have the following comments and concerns.

For generalised seizures since age 18 years the patient received levetiracetam (LEV) in a daily dosage of only 250 mg (Li, T. R. *et al.*, 2019). We should know why such a low dosage was chosen and if this low dosage contributed to the recurrence of seizures after one year. Was the low dosage chosen because of side effects, renal insufficiency, or low weight of the patient?

At age 19y, after recurrence of seizures, polypharmacy with LEV and lamotrigine (LTG) was initiated (Li, T. R. *et al.*, 2019). The authors claim that dosages of the antiepileptic drugs (AEDs) were adequate. We should know why LTG was added, which the maximal dosage of LTG was, and which the serum levels of LTG were.

For status epilepticus the patient received phenobarbital (PB) together with other AEDs, such as LEV and clonazepam (CLZ) (Li, T. R. *et al.*, 2019).

From PB it is well known that it is potentially mitochondrion-toxic (Finsterer, J. 2016). We should know if addition of PB resulted in deterioration of the phenotype in particular of epilepsy.

Since the patient underwent muscle biopsy, it would be interesting to know if also biochemical investigations for the activity of respiratory chain complexes were carried out. We should be informed which of the respiratory chain complexes had reduced activity. Since ND3 is part of complex-I of the respiratory chain we would expect complex-I deficiency.

Although the title indicates that the culprit mtDNA variant had occurred in a heteroplasmic distribution, there is no mentioning of the heteroplasmy rate in the results sections. We thus should know if heteroplasmy rates were determined by LFC-RFLP (Jackson, C. B. *et al.*, 2014) and if they were particularly high in damaged fibers seen on electron microscopy and harvested by microdissection.

The patient presented with bulbar manifestations, such as central facial palsy, tongue palsy, and dysarthria (Li, T. R. *et al.*, 2019). However, brainstem-evoked potentials were normal and cerebral MRI did not show a brainstem lesion (Li, T. R. *et al.*,

2019). We should know how the authors explained the bulbar manifestations.

MIDs are frequently multisystem disorders (Nesti, C. *et al.*, 2019). Thus, we should know if the presented patient was systematically investigated for subclinical or mildly manifesting involvement of any organ frequently affected in MIDs, such as the brain, eyes, ears, endocrine organs, heart, liver, intestines, kidneys, skin, bone marrow, or cartilage.

Patients with Leigh-syndrome or LLS frequently present with lactic acidosis of the brain (Krägeloh-Mann, I. *et al.*, 1993). Thus, we should be informed if lactate was determined in the cerebrospinal fluid (CSF) or if there was a lactate peak on MRS.

Overall, this interesting case could be more meaningful if heteroplasmy rates of various tissues were provided, if the patient was systematically investigated for multisystem disease, if single fiber studies were carried out, if bulbar manifestations were explained, if serum levels of LTG were determined, and if the low LEV dosage was explained.

REFERENCES

1. Finsterer, J. (2016). Toxicity of antiepileptic drugs to mitochondria. In *Pharmacology of Mitochondria* (pp. 473-488). Springer, Cham.
2. Jackson, C. B., Neuwirth, C., Hahn, D., Nuoffer, J. M., Frank, S., Gallati, S., & Schaller, A. (2014). Novel mitochondrial tRNA^{Ile} m. 4282A>G gene mutation leads to chronic progressive external ophthalmoplegia plus phenotype. *British journal of ophthalmology*, 98(10), 1453-1459.
3. Krägeloh-Mann, I., Grodd, W., Schöning, M., Marquard, K., Nägele, T., & Ruitenbeek, W. (1993). Proton spectroscopy in five patients with Leigh's disease and mitochondrial enzyme deficiency. *Developmental Medicine & Child Neurology*, 35(9), 769-776.
4. Li, T. R., Wang, Q., Liu, M. M., & Lv, R. J. (2019). A Chinese family with adult-onset Leigh-like syndrome caused by the heteroplasmic m. 10191T>C mutation in the mitochondrial MTND3 gene. *Frontiers in neurology*, 10, 347.
5. Nesti, C., Rubegni, A., Tolomeo, D., Baldacci, J., Cassandrini, D., D'Amore, F., & Santorelli, F. M. (2019). Complex multisystem phenotype associated with the mitochondrial DNA m. 5522G>A mutation. *Neurological Sciences*, 40(8), 1705-1708.