Molecular Genetics and Metabolism Reports 15 (2018) 127–128

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism Reports

journal homepage: www.elsevier.com/locate/ymgmr

Correspondence

Vaccination triggering onset of m.8993T > G associated Leigh syndrome

ARTICLE INFO

Keywords:
Renal
mtDNA
Mutation
Mitochondrial
Lactate
Multisystem disease

Letter to the Editor.

We read with interest the article by Uittenbogaard et al. about a 2yo male with maternally-inherited Leigh syndrome (MILS) due to the *ATP6* variant m.8993T > G at a heteroplasmy rate of 83% [1]. We have the following comments and concerns.

Normal development of the infant was interrupted by a vaccination with various vaccines at age 4 m [1]. Did the patient undergo CSF investigations after having developed floppy infant syndrome and was meningitis excluded? Why did the patient receive a second set of vaccines at age 6 m resulting in the inability of breastfeeding after the previous adverse reaction [1]?

Fig. 1 shows a significant increase of the size of the ventricles between age 4 m and age 9 m, suggesting hydrocephalus [1]. Cortical atrophy does not explain the dramatic dynamics, why it should be mentioned if the CSF pressure was increased and if the patient received a ventriculo-peritoneal shunt.

Infantile spasms (West syndrome) were treated with a combination of three antiepileptic drugs (AEDs) [1]. This unusual combination was obviously ineffective [1]. In a recent systemic review it has been shown that ketogenic diet may be beneficial in infantile spasms. Was ketogenic diet tried in the index case as well and was it beneficial? In addition to ketogenic diet and topiramat, West syndrome may respond to ACTH, steroids, and vigabatrim [2]. Were any of these alternative AEDs applied? In a study of 40 patients with infantile spasms, topiramat and levetiracetam were ineffective [3].

The variant m.8993T > G may not only manifest in the brain but also in the muscles [4], peripheral nerves (neuropathy), kidneys, or the eyes (retinitis pigmentosa, macular degeneration) [5]. Another feature may be hypocitrullinemia. Were any of these phenotypic features detected in the index case?

In summary, additional data about the cause of hydrocephalus, the treatment of epilepsy, and the phenotypic spectrum are eligible.

Conflict of interest

There are no conflicts of interest.

Funding

No funding was received.

Author contribution

JF: design, literature search, discussion, first draft, SZ-M: literature search, discussion, critical comments.

References

[1] M. Uittenbogaard, C.A. Brantner, Z. Fang, L.C. Wong, A. Gropman, A. Chiaramello, Novel insights into the functional metabolic impact of an apparent de novo m.8993T > G variant in the MT-ATP6 gene associated with maternally inherited form of Leigh Syndrome, Mol. Genet. Metab. 03 (Mar 27 2018) 011 (pii: S1096-7192(18)300647), https://doi.org/10.1016/j.ymgme.2018.

[2] J.M. Song, J. Hahn, S.H. Kim, M.J. Chang, Efficacy of treatments for infantile spasms: a systematic review, Clin. Neuropharmacol. 40 (2017) 63–84.

[3] A.A. Mahmoud, T.M. Rizk, A.A. Mansy, J.A. Ali, M.A. Al-Tannir, Ineffectiveness of topiramate and levetiracetam in infantile spasms non-responsive to steroids. Open labeled randomized prospective study, Neurosciences (Riyadh) 18 (2013) 143–146.

[4] Balasubramaniam S, Lewis B, Mock DM, Said HM, Tarailo-Graovac M, Mattman A,

https://doi.org/10.1016/j.ymgmr.2018.04.001
Received 3 April 2018; Accepted 4 April 2018

van Karnebeek CD, Thorburn DR, Rodenburg RJ, Christodoulou J. Leigh-Like Syndrome Due to Homoplasmic m.8993T > G Variant with Hypocitrullinemia and Unusual Biochemical Features Suggestive of Multiple Carboxylase Deficiency (MCD). JIMD Rep. 2017;33:99–107.

[5] K. Sofou, I.F.M. de Coo, E. Ostergaard, P. Isohanni, K. Naess, L. De Meirleir, C. Tzoulis, J. Uusimaa, T. Lönnqvist, L.A. Bindoff, M. Tulinius, N. Darin, Phenotype-genotype correlations in Leigh syndrome: new insights from a multicentre study of 96 patients, J. Med. Genet. 55 (2018) 21–27.

Josef Finsterer[a,*,1], Sinda Zarrouk-Mahjoub[b,1]
[a] *Krankenanstalt Rudolfstiftung, Vienna, Austria*
[b] *University of Tunis El Manar and Genomics Platform, Pasteur Institute of Tunis, Tunisia*
E-mail address: fifigs1@yahoo.de

* Corresponding author at: Postfach 20, 1180 Vienna, Austria
[1] Both authors contributed equally.