Pediatric Neurology 93 (2019) 64

Contents lists available at ScienceDirect

Pediatric Neurology

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

Correspondence

Management of *NARS2*-Related Mitochondrial Disorder is Complex

The article by Seaver et al. about two male infants with multisystem mitochondrial disorder (MID) due to a homozygous mutation in the *NARS2* gene is interesting.[1] Both children developed intractable epilepsy and died of multiorgan failure at ages three and nine months, respectively.[1] I have the following comments and questions.

Although avoiding valproic acid was an appropriate decision, it would be useful to know about the antiepileptic drug (AED) regimen in these brothers. Of particular interest is the type of AEDs applied, their maximal dosage, and the combinations that were tried. This is crucial because not only valproic acid but other AEDs such as carbamazepine, phenytoin, and phenobarbital, may be toxic to mitochondria.[2] If these agents were given in mono- or polytherapy, it is conceivable that they contributed to the intractability of seizures.

Interestingly, both patients presented with bilaterally symmetric hyperintensities of the occipitotemporal white matter on diffusion-weighted imaging.[1] Were these lesions hyperintense, isointense, or hypointense on apparent diffusion coefficient (ADC) maps? In other words, was there was cytotoxic or vasogenic edema? If the lesions represent impaired metabolism due to permanent seizure activity, paroxysmal activity on electroencephalography should be most pronounced over the occipitotemporal projections. But if they represent stroke-like lesions, they should show dynamic changes (expansion or regression) over time.[3]

Interestingly, both patients presented with unexplained thrombocytosis.[1] Was the thrombocytosis regarded as part of the phenotype or was it secondary to toxicity of the AEDs or an infection? In this respect, it is crucial to know if thrombocytosis was transient or permanent on repeated determinations. Because thrombocytosis has been previously reported as a feature of MIDs,[4] it can be regarded as inherent rather than as reactive.

Patient 1 experienced hypertrophic cardiomyopathy.[1] Cardiac involvement is common in individuals with MID but variable in other family members, so it would be interesting to know whether patient 2 was investigated for cardiac disease and whether he had hypertrophic cardiomyopathy or other cardiac abnormalities such as noncompaction, dilated cardiomyopathy, or histiocytoid cardiomyopathy.[5]

In summary, this report would be more meaningful if the authors can provide additional information about the AED regimen, cardiac investigations in patient 2, the nature of the diffusion-weighted imaging hyperintense lesions, and the cause of thrombocytosis.

References

1. Seaver LH, DeRoos S, Andersen NJ, et al. Lethal NARS2-Related Disorder Associated With Rapidly Progressive Intractable Epilepsy and Global Brain Atrophy. Pediatr Neurol. 2018 Aug 4. https://doi.org/10.1016/j.pediatrneurol.2018.07.014. pii: S0887-8994(18)30499-5.
2. Finsterer J, Zarrouk Mahjoub S. Mitochondrial toxicity of antiepileptic drugs and their tolerability in mitochondrial disorders. Expert Opin Drug Metab Toxicol. 2012;8:71–79.
3. Kim JH, Lim MK, Jeon TY, et al. Diffusion and perfusion characteristics of MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episode) in thirteen patients. Korean J Radiol. 2011;12:15–24.
4. Finsterer J, Frank M. Haematological abnormalities in mitochondrial disorders. Singapore Med J. 2015;56:412–419.
5. Finsterer J, Kothari S. Cardiac manifestations of primary mitochondrial disorders. Int J Cardiol. 2014;177:754–763.

Josef Finsterer, MD, PhD
Krankenanstalt Rudolfstiftung
Messerli Institute
Veterinary University of Vienna
Vienna, Austria
E-mail address: fipaps@yahoo.de.

Available online 27 November 2018

DOI of original article: https://doi.org/10.1016/j.pediatrneurol.2018.11.013.

Conflict of interest and source of funding statement: The authors declare no conflict of interest or financial disclosures concerning the materials or methods used in this study or the findings specified in this article.

Author contribution: J.F.: design, literature search, discussion, first draft.

https://doi.org/10.1016/j.pediatrneurol.2018.11.014