Reviewer’s report

Title: VARS2-LINKED MITOCHONDRIAL ENCEPHALOPATHY. TWO CASE REPORTS ENLARGING THE CLINICAL PHENOTYPE

Version: 0 Date: 26 Oct 2018

Reviewer: Marie Sissler

Reviewer's report:

In the present manuscript, C. Begliuomini and co-workers describe two new case reports of patients with mutations in the nuclear gene coding for the mitochondrial valyl-tRNA synthetase. The two patients have the rare homozygous c.1100C>T, p.Thr367Ile mutation, but with somewhat different clinical manifestations as compared to those previously described. These case presentations are of essential interest since they further exemplified the complexity of AARS2 related disorders.

As a very minor comments:
- Reference Kemp et al. 2011, may not be the most accurate one to define the fact that ValRS is a class I enzyme catalyzing the attachment of valine to its cognate tRNA molecule in a highly e-specific reaction.
- Could it be considered that the cardiomyopathy is not yet visible in the patients, but that it may occur over time since the two of them suffer from hypotonia?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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