Reviewer’s report

Title: Identification of a novel splicing mutation in the SLC25A13 gene from a patient with NICCD: a case report

Version: 0 Date: 04 Jul 2019

Reviewer: Duangrurdee Wattanasirichaigoon

Reviewer's report:

Dear the Editor of BMC Pediatrics

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The authors described a single case with mild jaundice. By using Next Generation Sequencing and gene panel of 137 known gene for cholestatic-typed liver diseases, the authors were able to identify a known pathogenic (c.852_855delTATG) and novel (c.1841+3_1841+4delAA) mutation of SLC25A13 gene, leading to definite diagnosis of NICCD in the patient.

Overall, the paper adds a novel mutation of SLC25A13 gene but does not provide in depth knowledge about their finding.

In addition, I had a chance to review this manuscript when it was submitted in March 2019. I found that some of my comment have not been responded appropriately as shown below.

Major comments

1) Case presentation:

- There is not enough information about differential diagnosis based on clinical presentation. Though we know that it is impossible sometime to give a diagnosis based on clinical data, but this is a single case report so the author should provide intellectual exercise what were potential etiologic diagnosis before jumping into genetic analysis.

- Though plasma amino acids (PAA) analysis was not performed, however PAA is not essential for confirmation of diagnosis. There are still several possible conditions that should be included in differential diagnosis.

- The author did not explain their finding well enough, such as, Page 6, line 56: "...which is predicted to probably affect RNA splicing by HSF (Supplementary Figure 1)". I would expect the author to provide how the novel mutation affect splice site, such as, the change/loss of splice score, how the mutant RNA sequence would be like and how that affect the protein. Thought it is not practical to perform RNA and Western blot analysis to confirm the effect of the mutation at RNA and protein level for new mutation of SLC25A13 because the gene is exclusively expressed in liver tissue and there is
multiple alternative splicing in the peripheral blood, at least the author should try to explain their new finding.

- According to the GenBank database and supplementary figure 1, the novel mutation identified should be c.1841+3_1841+4delAA (though the alternate name is NC_000007.13:g.95750964delTT).

2) Tables and Figures

- Table 2 and Figure 1 could be present as supplemental data

Sincerely yours,

Duangrurdee Wattanasirichaigoon, MD.

**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.

No

**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

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