Reviewer’s report

Title: Novel compound heterozygote mutations of TJP2 in a Chinese child with progressive cholestatic liver disease

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Reviewer: Teguh Haryo Sasongko

Reviewer's report:

The authors described a novel compound heterozygous mutation of TJP2 gene on a patient with PFIC. It has been known before that TJP2 mutations were found in a subset of patients with PFIC4. In its current format, the case report does not add to understanding nor clinical decision making in patients with PFIC. This manuscript may be published after a major revision:

1. The conclusion offered suggest a good addition to clinical decision making. However, the current content of the manuscript does not substantiate the conclusion. I would suggest the authors to provide a review of previous PFIC cases with TJP2 mutations. The review needs to answer if there is a pattern in the patients' clinical features to lead clinicians for TJP2 mutations.

2. Description of methodologies is especially lacking. I understand that an panel of 396 hereditary liver diseases genes were used. First, it is unclear if this is something that was developed/proposed by the authors or something which is already established. If it is the latter, there is no need to put the supplementary table and a proper citation would suffice. Second, there was no description of molecular workup (eg. from which tissue was the DNA extracted, brief information on the library prep, etc). Third, a brief but sufficient detail of the bioinformatics pipeline used is needed.

3. I suggest to validate the mutation findings with Sanger sequencing.

4. I wish to see the authors argue the value of the effort for doing NGS, given the cost and labor especially bioinformatics workup. Were the clinical features obtained not enough in directing the researchers to do more specific gene test? This needs to be discussed vis-a-vis clinical decision making.

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

No
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

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

No

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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None known
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