Reviewer's report

Title: Identification of two novel null variants of CLN8 by targeted next-generation sequencing: first report of a Chinese patient with neuronal ceroid lipofuscinosis due to CLN8 variants

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Reviewer: Conceicao Bettencourt

Reviewer's report:

Gao and colleagues present an interesting case report on a Chinese patient with NCL due to compound heterozygous mutations in CLN8. The results are sound and the authors also provide a literature revision on additional CLN8 cases. Yet, the manuscript would benefit from some revisions to make it clearer:

1) The manuscript would overall benefit from a thorough English revision for typos and grammatical errors.

2) In the first paragraph of the Background section all gene names should be in italics (CLN4/DNAJC5,…, and CLN3,…, are not).

3) The authors mention in Materials and methods that the NCL panel included 14 relevant genes, but only 13 genes are listed. This should be corrected. Also, as this study uses a target sequencing approach, the list of genes in the epilepsy panel should also be provided (at least as supplementary material).

4) In the Results section, the authors say that "CLN8 is the only gene with complex heterozygous variants". It is not clear whether among the filtered 16 rare SNVs were any homozygous variants. This should be clarified.

5) Although the authors found a plausible cause for the disease in the case they report, they should tone down on their statement at the end of the Results "So we summarized that the compound null mutations of CLN8 contribute to the NCL phenotype in this child.", and say something like "… mutations in CLN8 likely contribute to…".

6) In Table 1 the authors include p.Lys62del and p.Trp213del as being null mutations. However, these correspond to single amino acid deletions and would not automatically fit
the category of null mutations. The authors should reconsider their inclusion in the table. Also, the table legend should be completed (e.g. for what does CL/FP stand for?).

**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

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