Reviewer’s report

Title: A novel homozygous frame-shift mutation in the SLC29A3 gene: A new case report and review of literature

Version: 0 Date: 22 May 2019

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

RELEVANCE - Does this case report make a contribution to medical knowledge, have educational value, or highlight the need for a change in clinical practice or diagnostic/prognostic approaches?
Yes, this report contributes to medical knowledge

CASE DESCRIPTION - Are the details of the case sufficiently well described to understand the patient's symptoms and course of treatment?
Yes, the description of the case is sufficient

DIAGNOSIS/INTERPRETATION - Based on the facts presented, are the diagnosis, interpretation, and course of treatment medically sound?
Yes, the work described is medically sound

DISCUSSION OF THE CASE - Does the discussion appropriately analyse the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Has an adequate literature review pertinent to the case been included?
Yes, the case is discussed fully in the context of the literature

OVERALL MANUSCRIPT POTENTIAL - Could an appropriately REVISED version of this work represent a technically sound contribution?
Probably - with minor revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: The manuscript describes the discovery of a homozygous frameshift variant in SLC29A3 in 4 patients from two related families. It is presented as a case report with a review of the literature. The data itself is clear, but the text could use some help.

REQUESTED REVISIONS:
Major:
I would like to see the bioinformatics filtering steps used in the WES analysis or a short description of this. Given that it's a homozygous families, how many rare homozygous variants were present in the proband for instance?

Were any guidelines used for variation interpretation, such as ACMG? Were any bioinformatic approaches used for pathogenicity calling? This needs to be described.

There is no mention of public databases (with references). I assume that gnomad or exac were used, but what about the published Iranian genome? It is important to know that this homozygous variant was never found before in any public database, as it strengthens the association with disease. This needs to be described more clearly in the text.

The authors need to be more clear about who was heterozygous and who was homozygous for the frameshift variant. This is not clear from the text, but is clear in the figure.

The authors might want to include a phenotype table of the published mutations, as this helps give a more general view of the current data and phenotypes of SLC29A3 variations and helps the discussion.

Minor:
The English is readable, but needs to be improved.

May references are missing, eg p4 l87-88, p4 l92-93, p4 l97

ADDITIONAL REQUESTS/SUGGESTIONS:
if the authors include a full phenotype table of published mutations and use that to draw more conclusions from it, the manuscript could be expanded to a full version in my opinion.

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.

Yes

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:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

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