Reviewer's report

Title: Mutations in the PIGW gene associated with hyperphosphatasia and mental retardation syndrome: a case report

Version: 0 Date: 19 Feb 2018

Reviewer: Lydie Burglen

Reviewer's report:

Fu et al. report a new case of Hyperphosphatasia with mental retardation syndrome (HPMRS) related to mutations in the PIGW gene.

The report of this case could be the opportunity to make a review on HPRMS and share knowledge on this group of pathologies with the readers of BMC pediatrics.

Unfortunately, there are some mistakes and omissions in the paper that make it difficult to be published without major revisions.

Background: HPMRS may be caused by PIGV, PIGW, PIGO, and PGAP2, as described by the authors but also by PIGL (Fujiwara et al. Mutations in PIGL in a patient with Mabry syndrome, Am J Med Genet A. 2015;167A:777-85), PIGY (Ilkovskiet al. Mutations in PIGY: expanding the phenotype of inherited glycosylphosphatidylinositol deficiencies, Hum Mol Genet. 2015;24:6146-59) and PGAP3 (Howard et al., Mutations in PGAP3 impair GPI-anchor maturation, causing a subtype of hyperphosphatasia with mental retardation, Am J Hum Genet. 2014;94:278-87) mutations. These genes must be indicated.

Moreover, two articles reporting PIGW mutations, and not only one, have been published "Hogrebe et al., A novel mutation in PIGW causes glycosylphosphatidylinositol deficiency without hyperphosphatasia, Am J Med Genet A. 2016;170:3319-3322 must be added.

Case presentation:

Page 2, Ligne 45: please change "AKP" to "alkaline phosphatase (ALP)"

Because of the renal or cardiac malformations that are present in some HPMRS patients, it could be relevant to indicate the status of the patient regarding these organs.

Page 3, ligne 6: "psychomotor retardation" could be more relevant than "mental retardation".

Gene mutation analysis:

Page 3 ligne 40: please change "mutations" to "variants".
Moreover, it is necessary to discuss the possible pathogenicity of the variants (predicted pathogenicity by softwares of prediction, known or not in polymorphisms database, position in the protein, etc…), which are "of incertain significance", like noticed in the supplemental data. Since the pathogenicity is incertain (although the reviewer thinks that the variants are pathogenic, it is important to demonstrate it), a study of GPI-anchored proteins by quantification with multiparameter flow cytometry should be done in the patient (a low level is expected in the patient).

Page 3 ligne 47: the legends of the figure seem to be at the wrong place in the article?

Discussion:

Page 4 ligne 24: same comment than for background (genes involved in HPMRS)

Page 5 ligne 19: the level of alkaline phosphatase should be indicated in the case presentation section, not in the discussion.

Page 5 ligne 20: please change "mutations" to "likely pathogenic variants"

Page 5 ligne 23: the pulmonary disease of the patient should be a little more discussed. The brother had the same respiratory phenotype; what about the other patients in the literature? Never reported?

Bibliography: in addition to lacking reference, there are some typographic mistakes (lack of spaces between words, place of surname for example in ref1), a reference is duplicated (Krawitz 2010, ref 6 and 14) and the numbers in the text are not related to the good article (for example ref 13 is not about PIGW).

Supplemental data: Unfortunately, the reviewer could not judge if the data are relevant since the text is in characters that he is not able to understand.

**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.

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:

Needs some language corrections before being published

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

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal