Reviewer’s report

Title: Digenetic inheritance of SLC12A3 and CLCNKB genes in a Chinese girl with Gitelman syndrome

Version: 0 Date: 14 Dec 2018

Reviewer: Efstathios Koulouridis

Reviewer's report:

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GENERAL CONSIDARATIONS.

1. The question posed by the authors is well defined.

2. The methods are appropriate and well described.

3. The data are interestingly sound.

4. The discussion covers fairly the findings of the paper. Conclusions are relevant to the findings of the paper.

5. The title is misleading to the findings.

6. Abstract are relevant to the findings.

7. The writing is acceptable.

Minor Essential Revisions:

1. Abstract. Lines 31-34: If her grandmother has the same polymorphisms in SLC12A3 and CLCNKB genes why the grandmother doe's not suffer from Gitelman's syndrome phenotype?
2. According to your data patient's mother carried two SNP polymorphisms in CLCNKA c.1054-22(IVS11)delG, C and CLCNKB p.L94I. As you know inactivation of Barttin protein and digenic mutations affecting concomitantly CLC-KA and CLC-KB, in Barter syndrome type IV, which affect concomitantly the function of CLC-Ka and CLC-Kb, is coupled with the more severe clinical presentation of Barter syndrome. I would like to have your comment why these two polymorphisms did not act as "double hit" phenomenon and the mother did not exhibit any phenotypic evidence of salt loosing tubulopathy, except mild hypokalemia?

Compulsory Revisions:

1. Seyberth HW, in 2008, (Nat Clin Pract Nephrol 2008;4:560-567.) has proposed a new classification of salt loosing tubulopathies in three types: DC-type is referred to distal convoluted tubule dysfunction and comprises loss of function of NCC and CLC-KB. L-type is referred to the Loop of Henle dysfunction and comprises loss of function of NKCC2 and ROMK, and the L-DC type which comprises a mix category with loss of function of CLC-KA and/or CLC-KB and the b-subunit Barttin. Taken in account that your patient exhibits a phenotype relevant to Gitelman syndrome but her genetic abnormality comprises a polymorphism in SCLC12A3 (characteristic of Gitelman syndrome) and a polymorphism in CLC-KB (characteristic of Bartter syndrome) it is more proper to reassume your terminology and classify your case according to Seyberth's terminology and not the classical terminology.

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:

Acceptable

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