Reviewer's report

Title: Complicated Gitelman syndrome and autoimmune thyroid disease: A case report with a new homozygous mutation in the SLC12A3 gene and literature review

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Reviewer: Marek Saracyn

Reviewer's report:

Dear Authors,

The paper titled: „Gitelman Syndrome complicated with autoimmune thyroid disease: A case report with a new homozygous mutation in the SLC12A3 gene and literature review” by Haiyang Zhou et al. aimed to

(1) present a rare case of coexistence the Gitelman Syndrome (GS) and Grave's Disease (GD)
(2) review the update literature to discuss this phenomenon.

The authors have come to the conclusion, that GS associated with hyperthyroidism can cause hypokalemic periodic paralysis and their patient was misdiagnosed with hypokalemic periodic paralysis for a long time, indicating that there is a need to consider the possibility of GS in clinical cases with hyperthyroidism and persistent hypokalemia.

The paper is generally well designed, well presented and the conclusions are potentially of a certain interest.

There are however some issues that should be addressed:

1. Title: As you correctly assume, you do not know whether the GS is complicated by ATD/GD or not, because we still do not know common precise genetic mechanisms both diseases. Now, we can only confirm the natural co-existence both diseases. So, the title must be slightly changed.

2. Abstract: Potassium supplementation can not be enough, when potassium concentration (not level) is decreased. As above, we do not know, whether the GS is associated with ATD/GD or not. In other words you did not prove it in your paper. Key words should be in accordance
with Medical Subject Headings in PubMed (http://www.ncbi.nlm.nih.gov/pubmed), please verify them. The hypokalemia (hypokalaemia) not a kaliopenia.

3. Background: As above, not "… patient with GD complicated with GS…", but e.g. "… patient with GD and GS…"

4. Case: Potassium citrate is not the best choice of treatment, because it can escalate the metabolic alkalosis. Don't you think, the patient needs a radical treatment of GD? Did you plan it? Uncontrolled hyperthyroidism in this patient probably exacerbates the symptoms of GS.

5. Discussion:
- Is the incidence of GS in Japanese population 10.3/10000 or 10.3/100000?, because further you give all incidence per 100 000? This information will have some influence on the conclusions - the same or 10-fold lower incidence of GS than GD?
- What about the possible links between iodine and potassium metabolism, as you nicely described an iodine and magnesium links?
- The hypokalemia in your case was really deep. Don't you think, that it can be another reason for such hypokalemic state? I mean, in the discussion section at least you should mention about other possible causes of hypokalemia in your case - channelopathies (defects of CACNA1S, SCN4A, KCNE3) - as a common causes of hypokalemic periodic paralysis.
- In the discussion you should also try to answer for the most interesting question: are there possible join points in the molecular pathogenesis of GS and GD/ATD? I mean, a common genetic pathomechanisms or at least close chromosomal localization of the GS causative gene (SLC12A3) and possible GD loci (CTLA-4, MHC2, variants of THSR, TG, etc.)

6. Conclusion: As above, …. GS is not associated with….

You do not describe the case with hypothyroidism, but with GD. So, the conclusions must be slightly corrected.

7. Table 3: Why there is so deep hypothyroidism on the last follow up visit (12thDec)? You did not mention it in the Case section.

8. There are several misspelling and grammar errors. Please go through the paper thoroughly.

10. Finally, considering the whole paper, your manuscript might be accepted for publication in the BMC Endocrine Disorders pending changes mentioned above.
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?
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