**Reviewer’s report**

**Title:** Isolated hypoaldosteronism as first sign of X-linked Adrenal Hypoplasia Congenita caused by a novel mutation in NR0B1/DAX-1 gene: a case report.

**Version:** 0  **Date:** 31 Mar 2019

**Reviewer:** Daniel Konrad

**Reviewer's report:**

Iughetti et al. report on a boy with a novel mutation in the NROB1/DAX-1 gene presenting with salt wasting at the age of 5 weeks.

In general, this is an interesting case report since the boy presents with salt loss with little clinical and laboratory signs for glucocorticoid deficiency.

**Comments**

1) The identified mutation in the NROB1/DAX-1 gene is reported to be novel. What is the predicted consequence of the mutation, i.e. is it predicted to be pathogenic? Moreover, was a database and/or controls screened to exclude that the mutation is not a (rare) DAX-1 variant?

2) How were blood glucose levels at the time of salt loss? Low glucose levels can be a sign of manifest glucocorticoid deficiency.

3) Gonadotrophin and testosterone levels are still within normal limits for the age of 9 months and due to mini puberty. These findings should be commented accordingly.

4) Adrenal auto-antibodies were determined to exclude adrenal insufficiency due to autoimmunity? However, this seems to be a very unlikely cause for the child given the first presentation at an age of 5 weeks.

5) A table is presented summarizing recent case reports of DAX-1 mutations. The recent published paper by Gerster K et al (JPEM 2018) should be added to that list.

**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

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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