Reviewer’s report

Title: Spontaneous Fertility and Variable Spectrum of Reproductive Phenotype in a Family with Adult-Onset X-Linked Adrenal Insufficiency Harboring a Novel DAX-1/NR0B1 Mutation

Version: 0 Date: 28 Dec 2019

Reviewer: Emilio Fiore

Reviewer's report:

In this work the authors report a novel DAX-1/NR0B1 mutation in members of a family affected by late onset X linked adrenal hypoplasia congenital (AHC). They describe a very late onset form of AHC with variable hypogonadal and reproductive features including spontaneous fertility observed in two members of the family. For this reason the authors suggest that NR0B1 mutation carriers, even those that are allegedly asymptomatic, should be carefully monitored, with periodical exams, including spermograms and early sperm banks in order to warrant fertility preservation on AHC males and diagnose very late primary adrenocortical insufficiency.

Comments

a) Figure 1A is a low resolution image and it is not clear.

b) How many members of this family (both males and females) were tested to rule out primary adrenocortical insufficiency?

c) Was any case of delayed puberty described in this family?

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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