Reviewer’s report

Title: A putative role for the aryl hydrocarbon receptor (AHR) gene in a patient with cyclical Cushing’s disease

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Reviewer: Craig Tomlinson

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Paper Review for BMC Endocrine Disorders
Date: 09/10/2019

Full Title: A putative role for the aryl hydrocarbon receptor (AHR) gene in cyclical Cushing's disease
Manuscript Number: BEND-D-19-00294R1

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The authors have submitted a case report describing an association between a germline mutation in the AHR gene and cyclical Cushing's disease. Exome sequencing of germline and tumor DNA from a 47-old male patient led to the finding. Other bench and in silico methods showed that the mutation is at a putative phosphorylation site on the AHR that is hypothesized to be the mechanism that prevents translocation of the AHR into the nucleus and presumably subsequent AHR transcriptional activity. Criteria for acceptance of a case study in BMC Endocrine Disorders include findings that shed new light on the possible pathogenesis of a disease and the identification of possible new associations in disease processes. The case study here satisfies these criteria. Little is known or has been investigated regarding cyclical Cushing's disease, and although the work is relatively slight, which is often the situation for case studies, it advances the field.

Reviewer's conclusion: Acceptance with minor revisions.

Suggested minor revisions.

1. AIP is not a ligand of the AHR. AIP is an AHR chaperone.

2. Descriptions of other studies are not referenced or are referenced later in the paper. For example, several times the AHR phosphorylation site is mentioned in the paper without reference. The means by which the phosphorylation site is called is finally cited in a figure legend. Each mention of a finding from a published study/method should be appropriately cited.

3. Not a suggested revision, but it would have been helpful if there had some sort of marking to indicate where and what revisions were made in the revised version (revised portions marked in yellow for example).
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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