**Reviewer’s report**

**Title:** A case of autonomous cortisol secretion in a patient with subclinical Cushing’s syndrome, GNAS mutation, and paradoxical cortisol response to dexamethasone

**Version:** 0  **Date:** 02 Sep 2018

**Reviewer:** Maria Fragoso

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The authors described a Case report with mild adrenal hypercortisolism. The authors called attention for the paradoxical increasing 24 h urinary cortisol response to the dexamethasone suppression test in a patient with somatic GSP mutation.

Major comments about the manuscript number BEND - D - 18- 00232

1) The title should be more clearly related to the case. Once the discussion of the manuscript is about the strange case and not about the mechanism involved in the paradoxical increasing urinary 24 h cortisol after DST.

2) In the title, the authors used Cushing syndrome (Cushing's syndrome is correct form) and in the abstract, the authors used subclinical Cushing syndrome (Cushing's syndrome is correct form). Important to define if the patient presented autonomous cortisol-producing or potential cortisol or classical overt Cushing's syndrome, according new guideline.

3) Pag 2 line 45 - The authors should specify which neoplasia is present in the different sites and which type of skin pigmentation was present.

4) Pag 2 line 47 - Which cortisol was increased in response to v.o. dexamethasone (missing the administration) (urinary ?, salivary ?, serum ?) …

5) Pag 2 line 49 - Which cortisol persisted in response to v.o. dexamethasone (missing the administration) (urinary ? salivary ? serum ?) after adrenalectomy?
6) Pag 2 Only in the conclusions the authors commented about mixed producing cortisol and androgens.

7) Th authors concluded that the paradoxical response of cortisol is due to GNAS mutation without any study in this issue.

8) The authors concluded that there is an association with somatic adrenal mutation of GNAS and the others neoplasias of the patient without a GSP screening of GSP mutation on the different sites. In addition, wrote that these findings could improve the prognosis of patients with Cushing's syndrome ?? It does not make sense.

9) Page 3 line 93 - Did the urinary free cortisol was measured by LC-MS/MS?

10) Page 4 - Table 1 - I did not see the androgens level and also 24h urinary free cortisol referred by the authors.

11) Did the patient present criterions for primary aldosteronism?

12) Once the histology is in accordance with primary macronodular adrenal hyperplasia why the authors identified such as adenoma? page 11 figure 3 - compact cells and clear cells

13) Did the patient present criterions for McCune Albright syndrome? The authors should comment on this.

14) The authors should improve the English language.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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.

No

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:

Needs some language corrections before being published

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