Author's response to reviews

Title: Cushing syndrome secondary to ectopic adrenocorticotropic hormone secretion from a Meckel diverticulum neuroendocrine tumor: Case report

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Author's response to reviews: see over
Dear Editors:

Please find enclosed our response to the reviewer’s comments as well as the revised version of the manuscript entitled: “Cushing syndrome secondary to ectopic adrenocorticotropic hormone secretion from a Meckel diverticulum neuroendocrine tumor” by Diana Loreta Paun et al. that we are submitting for consideration to BMC Endocrine Disorders.

We would like to thank Professor Karsten Müssig for his constructive and positive opinions, advice and requests that we have taken in consideration in the revised manuscript and figures.

Please find below our answers to the reviewer’s comments:

Line 84: Relative time data should be given.
The patient noticed weight loss and complained of extreme fatigue and muscle wasting over the five months preceding his first hospitalisation. Time data were included in the manuscript at line 84.

• Line 86: Weight reduction as percentage of initial body weight and the time period in which the weight loss occurred should be added.
This information is now added, as requested.

• Line 92: Was a CRH test performed?

Indeed, the two dynamic tests with highest diagnostic sensitivity in favour of the EAS-CS diagnosis are CRH stimulation test (with a considered sensitivity ranging to up to 93% (Nieman LK, J Clin Endocr Metab 1993)) and high dose dexamethasone suppression test. Although, very sensitive,
we could not perform a CRH test, as CRH is not available and not authorised by the National (Romanian) Drug Agency.

- Line 104: "DM" should be replaced by “diabetes mellitus”.
  We thank the reviewer for this suggestion; the term is now extended in the revised version.
- Line 104: The dosage of metformin should be added.
  Metformin dosage was added in the revised manuscript, as requested.
- Line 106: The dosage of calcium and vitamin D should be added.
  Both calcium and vitamin D dosages were also added in the revised version of the manuscript.
- Line 114: Immunohistochemical staining for somatostatin receptors should be added.
  We did not consider necessary to perform somatostatin receptor immunostaining as scintigraphy with 99mTc-labelled somatostatin analogs was intensively positive and functionally confirmed the tumor somatostatin receptor high content. Indeed, patient’s evolution while treated with sandostatin was also favourable with satisfactory control of hypercortisolism. However, as requested, we tried to perform somatostatin immunostaining, unsuccessfully, as we were not able to acquire a functional and specific antibody.
- Lines 118 und 119: "carcinoids" should be replaced by “NET”.
  We thank the reviewer for this correction.
- The manuscript should be proof read by a native English speaker in light of the grammar errors within the text, such as line 128 “this patient progression free survival” or lines 131 and 136 use of “whether” instead of “while”.
  The manuscript was reviewed by several correctors and grammar and vocabulary were revised.
- Table 1:
  o “Natraemia” should be replaced by “Sodium”.
  o “Kalimemia” should be replaced by “Potassium”.

“glycaemia” should be replaced by “glucose”. Was it a fasting glucose? These terms have been corrected as suggested. The table contains fasting glucose values.

The reference range of sodium should be added.

We thank the reviewer for having noticed missing Na reference values in the table which is now corrected.

The used abbreviations should be explained in a footnote.

- Figure 1:
  - “Axial” should be added to the images in the first row.
- Figure 2:
  - Relative time data should be given.
  - The axis for CgA should be added.

We have revised the two figures, as suggested and also explained the used abbreviations.

We hope you will find satisfactory this revised version of the manuscript, and would be pleased to provide you with any further information you may require.

Sincerely yours,

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