Author’s response to reviews

Title: Extensive ARMC5 genetic variance in a case of primary bilateral macronodular adrenal hyperplasia started with exophthalmos: a case report

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Author’s response to reviews:

Dear Dr. Bernhard Schaller

Thank you very much for your decision letter and advice on our manuscript (Manuscript JMCR-D-17-00725) entitled “Extensive ARMC5 genetic variance in a case of primary bilateral macronodular adrenal hyperplasia started with exophthalmos: a case report”. We also thank the reviewers for the constructive and positive comments and suggestions. Accordingly, we have revised the manuscript. All amendments are highlighted in yellow in the revised manuscript. In addition, point-by-point responses to the comments are listed below this letter.

We hope that the revision is acceptable for the publication in your journal.

Look forward to hearing from you soon.

With best wishes,

Yours sincerely,
First of all, we would like to express our sincere gratitude to the reviewers for their constructive and positive comments.

The case report is an interesting one. However the title and the contents say that exophthalmos was the presenting feature and a lot of emphasis has been placed on that which should be changed. Exophthalmos due to retrobulbar fat deposition is an important feature of hypercortisolism due to any cause and is not limited to primary bilateral macronodular adrenal hyperplasia. Further the clinical suspicion of hypercortisolism occurs when the additional clinical features like central adiposity, proximal myopathy, broad dehiscent purple stria, moon facies, buffalo hump etc show up so undue emphasis on exophthalmos is unwarranted.

Response: Thank you for your insightful suggestion. There are several reasons why I emphasized on exophthalmos in our case report. First, although exophthalmos is seen in about 30–45% of patients with Cushing’s syndrome (CS), it is typically associated with Graves’ ophthalmopathy. In our case, the patient was also treated as Graves’ ophthalmopathy at the beginning when she had no clinical features of CS. Second, Although first described in 1932 by Harvey Cushing in 4 of his 12 patients with Cushing’s disease, exophthalmos is a forgotten clinical sign of CS at this time. Third, as reported, severe exophthalmos can also precede the evolution of CS. Early recognition of atypical symptoms like exophthalmos in patients with CS can avoid the risk of long-term exposure to the detrimental tissue-catabolic effects of cortisol excess. It is the contribution to the medical literature. I also revised this discussion section (please see the highlighted text).

The values for the diurnal rhythm of cortisol and ACTH should be provided.

Response: Response: Thank you for your insightful suggestion. We have provided the values for the diurnal rhythm of cortisol and ACTH in the Case presentation section (please see the highlighted text)
Spellings of Endocrinology, Cushingoid and Exophthalmos need to be corrected at various places.

Response: Correction has been made in the revised manuscript (see the highlighted text).