Reviewer’s report

Title: A case of Adrenocorticotropic hormone -independent bilateral adrenocortical macronodular hyperplasia concomitant with primary aldosteronism

Version: 0 Date: 30 Jun 2017

Reviewer: Silvia Monticone

Specific comments

- Despite the final diagnosis of left unilateral PA seems to be quite convincing, my criticisms are confined predominantly to the choice made by the authors of normalizing adrenal vein aldosterone levels for cortisol, regardless of the diagnosis of Cushing's syndrome. The presence of autonomous cortisol overproduction could significantly affect both the selectivity index and the lateralization index leading to inappropriate adrenalectomy. As acknowledged by some authors (Burrello J, HMR 2016), correcting for plasma metanephrines would be more appropriate. Together with the cortisol levels it would be interesting to have also the measurements of plasma metanephrines in the IVC and in the adrenal veins. If this is not possible, the authors should mention this aspect in the discussion.

- The units used for cortisol measurement are incorrect. Should it be µg/dL (instead of mg/dL)?

- Please provide an additional table indicating the type and dilution of used antibodies for the immunohistochemical studies

- Please provide a low magnification picture of the CYP11B2 immunostaining. Was the immunoreactivity localized to the aldosterone producing cell clusters only or other CYP11B2 adrenal nodules could be detected?
Mutations in the ARMC5 gene have been identified in both AIMAH and African American patients with primary aldosteronism. It would be extremely interesting to know if this patient has any mutation in ARMC5 that could explain the coexistence of the two conditions.

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:

Not suitable for publication unless extensively edited
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