Reviewer’s report

**Title:** An unusual case of ectopic corticotrophin-releasing hormone syndrome caused by an adrenal noncatecholamine-secreting pheochromocytoma: a case report

**Version:** 0 **Date:** 25 Nov 2017

**Reviewer:** Irina Bancos

**Reviewer's report:**

Authors present a rare case of ectopic Cushing syndrome due to CRH production from an otherwise non-functioning pheochromocytoma.

- This case presentation would benefit from a higher level of detail in regards to patient's clinical presentation - hirsutism, menstrual cycle, the degree of weight loss, a more extensive family history of pheochromocytoma/paraganglioma, any genetic testing for mutation predisposing to pheochromocytoma (this young woman is certainly at risk for a genetic cause of pheochromocytoma).

- What was the reasoning for the initial ultrasound 16 months prior to presentation?

- Authors argue that dexamethasone administration triggered CRH production marking the onset of severe hypercortisolism and its clinical consequences. However, patient's clinical presentation just 4 weeks after dexamethasone makes this theory somewhat unbelievable. This young woman had developed hyperpigmentation, significant muscle atrophy, adipose redistribution and other symptoms suggestive of hypercortisolism longer than 4 weeks, though possibly not as severe. While I think that dexamethasone theory can stay in the manuscript, I would like to suggest to tone down the confidence level on this association.

- This patient presented with a very severe life threatening hypercortisolism, and the urgency of rapid evaluation and treatment should be underlined. I suggest to include the timeline from biochemical confirmation of cushing syndrome to therapy, any discussion of any possible delays
in this therapy. Patient had several evaluations which were not completely necessary - such as
dexamethasone suppression test in this clearly severe cushing, work up for differential causes of
diabetes ( when steroid induced hyperglycemia was very high on the list), and other. I would
suggest rewriting the sequence events and possibly taking away the unnecessary details in
evaluation.

- Per discussion, it seems to me that authors did treat this patient with prednisone after surgery,
however case description does not describe it. ACTh drop after surgery was described - what
about cortisol?

- These are my preliminary comments, will be glad to relook at the manuscript again once
addressed

**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

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No

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