Reviewer’s report

Title: Late-onset isolated adrenocorticotropic hormone deficiency caused by nivolumab: a case report

Version: 1 Date: 19 Dec 2017

Reviewer: Hideaki Miyoshi

Reviewer's report:

This is a case report of isolated adrenocorticotropic hormone deficiency occurred six months after the discontinuation of nivolumab. The results are clinically informative and important as a caution, but some comments should be addressed.

Comments to the author

Minor points

1. Authors only showed Ipilimumab, as CTLA-4 antibody and nivolumab, an anti-programmed cell death protein 1 (PD-1) antibody agents in "Background" and "Discussion and conclusions". However, now various immune checkpoint inhibitors (tremelimumab (CTLA-4) and pembrolizumab (PD-1 antibody), for example) can be used other than Ipilimumab and nivolumab. The description should be arranged. Are there any reports focused the difference in the incident rate of isolated ACTH deficiency or other side effects among those CTLA-4 or PD-1 antibody agents?

2. The diagnosis is one of the important key point for this case presentation. However, there is only one sentence, "The responses of ACTH and cortisol to corticotrophin-releasing hormone were disappeared, although the responses of other anterior pituitary hormones were normal." as the diagnosis of isolated ACTH deficiency. Please add the information more detail.

3. In Figure 1, it seemed that the supplementation of steroids did not start immediately after sodium declines became apparent, and hydrocortisone was administered after the sodium level further declined. Why hydrocortisone did not administer immediately? And it is difficult to grasp the time course and relationship among malaise and appetite loss, hyponatremia, and hypoglycemia. Add more description to the report or figure 1.

4. Is there a possibility thyrotoxicosis or hypothyroidism influence the occurrence of isolated ACTH deficiency.

5. Continuous monitoring of serum sodium level is actually important, but symptomatic sign of hyponatremia is also important as this patient admitted to the hospital from the chance of the symptoms. Giving the information about the possible signs and caution period to patients who use it, is also important. Please include that.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Unable to assess

Does the work include the necessary controls?
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Unable to assess

Are the conclusions drawn adequately supported by the data shown?
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Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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Not relevant to this manuscript

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