Author's response to reviews

Title: Syndrome of Inappropriate Antidiuretic Hormone (ADH) Associated with Ectopic ADH-secreting Gastric Adenocarcinoma: a case report

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Reviewer 1

This manuscript includes many of the essential features of SIADH with hyponatremia, hypouricemia, concentrated urine, high urinary sodium concentration and increased plasma ADH levels in a patient with normal renal, thyroid and adrenal function. This manuscript can be improved by stating that all of these findings minus the ADH presence in carcinomatous tissue can be found in a patient with renal salt wasting (RSW), a term that should supplant cerebral salt wasting because renal salt wasting has been demonstrated conclusively in patients without cerebral disease. The major strength of this manuscript is the demonstration of ADH being present in the carcinomatous tissue and not in normal gastric cells. Differentiation between SIADH and RSW on first encounter is extremely difficult to make because clinical assessment of the volume status of such patients is extremely inaccurate and unreliable. This differentiation is imperative to make because of divergent treatment goals, fluid restrict for SIADH and administer salt and water for RSW. ADH levels in both conditions can be elevated except for being appropriately increased in RSW and not so in SIADH. Removing the volume stimulus for ADH secretion in RSW can be accomplished with volume repletion with saline, which was not addressed in this patient, as saline would induce excretion of dilute urines and correction of hyponatremia. This diagnostic and therapeutic dilemma should be addressed in this manuscript.
with the conclusion that while SIADH could not be differentiated from RSW in this patient, the ectopic presence of ADH in the gastric tumor would strongly favor the diagnosis of SIADH.

- We appreciate your comments. We totally agree with your suggestions of ambiguity between renal salt wasting and SIADH in clinical conditions. However, as you suggest, we confirmed the presence of ADH secretion in tissue and hyponatremia partially and completely recovered after water restriction and gastrectomy. These findings are consistent with SIADH in our patient. Furthermore, we did not know any report of cancer associated renal salt wasting syndrome.

Reviewer 2

1) The authors showed normal gastric tissues stained with anti-ADH antibody as negative control, but tissue from gastric adenocarcinoma patient not presenting SIADH is more appropriate as negative control. If the control IgG is available, gastric tissue from the presented case stained with control IgG is also appropriate as negative control.

- To our regrets, we did not use negative control as other tissues not presenting SIADH. Additionally, control IgG is not available. However, previous report also did not use negative control (Nakayama et al. Endocrine. 2009;35:290-2). We used antibody from same company for immunohistochemical staining. We think that it is sufficiently meaningful to stain gastric tissue in our patient to prove the presence of ADH secreting cells.

(2) As the authors described in the report, there are very few reports showing association between SIADH and gastric cancer. That means gastric adenocarcinoma presenting SIADH is very rare. If so, the author's conclusion that "gastric cancer should be included as a differential diagnosis of cancer with SIADH" seems not proper conclusion.

- We totally agree your suggestion. We did change our conclusion into other expressions.

(3) Mistakes about English diminish the value of this report. Please check English again carefully. The very first sentence in the report is already wrong.

- We already checked our manuscript for “English” into www.textcheck.com. We carefully checked our “English” again with the help of specialist.