Reviewer's report

Title: A case report of syndrome of inappropriate antidiuretic hormone secretion with Castleman's disease and lymphoma

Version: 1 Date: 19 November 2012

Reviewer: Pascal Meier

Reviewer's report:

Major compulsory revisions
1. The lab findings of the patient presented the following values: serum sodium: 112 mmol/l, chloride: 81 mmol/l, effective osmolality at 267 mOsm/kg.H2O, urinary sodium: 85 mmol/l, chloride: 86 mmol/l and osmolality: 257 mOsm/kg.H2O during hypotonicity with normal dietary salt intake. Although these lab values may correspond to a SIADH, some other criteria are needed to ascertain this diagnosis such as:
   a. Serum uric acid <4 mg/dL (<0.24 mmol/L)
   b. Blood urea nitrogen <10 mg/dL (<3.57 mmol/L)
   c. Fractional sodium excretion >1%; fractional urea excretion >55%
   d. Failure to improve or worsening of hyponatraemia after 0.9% saline infusion
   e. Improvement of hyponatraemia with fluid restriction
   The authors should precise their diagnosis of SIADH including the above-mentioned criteria.

2. Diseases classified as typically associated with low urine [Na+] may present with high urine [Na+]. Consequently, urinary sodium excretion should be used cautiously as a diagnostic marker in patients with supposed SIADH. In these patients, fractional uric acid excretion (FE-UA) can instead be used to aid the differential diagnosis of hyponatraemia, particularly in differentiating between SIADH and hypovolaemic hyponatraemia (an FE-UA cut-off value of 12% appears to be optimal to confirm the diagnosis of SIADH [positive predictive value of 100%], whereas an FE-UA <8% excludes SIADH). Spot urine sodium measurements are not always accurate but are often all that is available in the early assessment of hyponatraemia. This is the reason for the grey area in the algorithm, between 20–40 mmol/L. The authors should consider this remark in the evaluation of SIADH.

3. If the authors consider a clear-cut relationship between SIADH and a B cell lymphoma, previous case reports related to this association have already been published:
b. Yuji Hirata et al. Leukemia & Lymphoma, 2009; 50(7): 1226–1229


e. Kokichi Morimoto et al. DOI: 10.2169/internalmedicine.46.0252

f. …

They should clearly propose some new mechanistic hypotheses explaining the role of the B cells and the SIADH or present new data such as the place of the polyclonal Castleman’s disease and its relationship with the lymphoma.

4. Unfortunately there are some inaccuracies when considering the correction of the SIADH once the patient was treated. Which role had really played the chemotherapy? The authors should precise the time course of the fluid restriction that is often the standard of care in patients with asymptomatic hyponatraemia secondary to SIADH.

5. There is some confusion regarding the potential etiology of the SIADH. Is there the B-cell lymphoma the real cause of the SIADH or does the Castleman’s disease (that needs to be proven) represent the etiology of the SIADH (one case reported so far: ref 7)?

Minor essential revision

1. The patient’s case presentation should be more precisely exposed, i.e. time-course of the SIADH evolution regarding to the treatment, ascertain the biological values (Table), the details of the herniation of suprasellar cistern, the supposed hypopituitarism …

2. Too many figures are presented and do not add much to the comprehension of the case.

Discretionary revisions

1. The authors should expose some personal hypotheses to explain their case.

2. Some mechanistic hypotheses are needed to try to understand the relationship between the lymphoma, the Castleman’s disease and the SIADH.

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.