Reviewer's report

Title: 1,25 Dihydroxyvitamin D and PTHrP Mediated Hypercalcemia in a Seminoma

Version: 1 Date: 15 January 2014

Reviewer: Bruno Ferraz-de-Souza

Reviewer's report:

Rodriguez-Gutierrez et al. have prepared a succinct manuscript describing an interesting facet of seminomas, namely calcitriol- and PTHrp-dependent hypercalcemia. This article should be of interest to endocrinologists and specialists in bone metabolism, as well as to a broader medical readership.

Minor Essential Revisions:

1) The manuscript would benefit from language revision by a native English speaker. For example, the sentence starting with “Creatinine was” on page 5, 2nd paragraph, needs to be rewritten; Page 7, 1st paragraph, 6th line, verb is repeated;

2) The authors should avoid the repeated claims of this being the “first documented” report of its kind; indeed, this information should be removed from the abstract;

3) Page 5: ultrasound report needs to be more detailed: hypo/hyperechogenic suggests heterogeneity and should be better defined;

4) Page 6: the calcium-lowering therapy with calcitonin and hydration is described as “aggressive” – this is an overstatement, as additional measures (furosemide, intravenous bisphosphonates) could have been taken. The adjective should be removed;

5) Page 7, discussion of malignant hypercalcemia: in mechanism number 1, what does the “20% of cases” apply to? To osteolytic metastases or to breast cancer? Please clarify in the text;


7) Page 9: the sentence opening the paragraph on the mechanisms of calcitriol secretion by tumors is misleading and needs to be revised: there is no debate as to how calcitriol leads to hypercalcemia, but indeed there is uncertainty (as the authors rightly discuss ahead) as to how calcitriol is produced;

8) Page 9: in the last sentence, it is stated that 24h calciuria was normal but values are not adjusted by weight (mg/kg/d) – does it fall within 2-4 mg/kg/d?
Indeed, it would be better to state 24-h calciuria in mg/kg/d in Table 1;

9) Had the patient been previously diagnosed with cryptorchidism? The authors should include a mention to cryptorchidism as a mechanism predisposing for seminomas in the discussion;

10) Last sentence of discussion: it is a too big statement to claim that calcium-lowering medications should be withheld until definitive treatment for seminomas based on such small numbers of cases - this statement has to be softened;

11) Interestingly, the patient had normal serum phosphorus in presence of PTHrp excess – this should be discussed;

12) References: there is no calling to reference 17 in the text;

13) Legend to Figure 1 needs to be improved with better description of mass (dimensions, etc) and definition of what the white arrow is pointing towards

14) Table 2:
--- reference numbers do not match manuscript references;
--- last row appeared out of frame with rows above;
--- it would be more useful to show post-treatment Ca levels rather than state it was normal in all reports;
--- NM might not be appropriate: even though values were not stated in the previous reports, they might have been made – please change to NS, not stated;
--- please define CT in legend.

Discretionary Revision:

The title would be more clear as “Malignant hypercalcemia mediated by 1,25-dihydroxyvitamin D and PTHrp in a patient with a seminoma”.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I declare that I have no competing interests