Reviewer’s report

Title: Coexistence of pernicious anemia and prostate cancer: an experiment of nature involving vitamin B12 modulation of prostate cancer growth and metabolism: a case report

Version: 4 Date: 21 April 2009

Reviewer: Lauren Harshman

Which of the following best describes what type of case report this is?: Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Has the case been reported coherently?: No

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: No

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: No

Will the case report make a difference to clinical practice?: No

Is the anonymity of the patient protected?: Yes

Comments to authors:

Overall, this report is an interesting observation between pernicious anemia, progressive prostate cancer, and a possible rise in PSA after corrective treatment for the anemia. But I do think there is a significant amount of missing data that I would like to see before recommending publication; most importantly the trajectory of the anemia (i.e., what was the hgb and MCV at diagnosis of the prostate cancer and of the rise in PSA after 10/30/08 or in early 2009.

Specific comments:

A. Abstract:
1. Last line of first paragraph, "...B12 were associated with a rapid increase of PSA..." I think the term 'associated' implies causation and do not think it is appropriate as this could merely be a coincidental event.

2. The phrase ‘experiment of nature’ is confusing to me. What does that mean?

B. Introduction
1. Missing word: represents the majority “OF” measurable

2. Please clarify: “…33% to be holotranscobalamin insufficient…” So the general reader does not have to look up the reference themselves, please clarify the sentence with the following: Is it 33% of prostate cancers or all cancers? What is the sample size of the population studied?

3. Last sentence of paragraph 1 is awkward, would remove “the deficiency of”

4. 2nd paragraph. Use of the term “excesses” is awkward.
   - In the first sentence, do you not mean, “associated” with increased rates pernicious anemia.”? Would put the reference notation after this sentence.
   - An excess of gastric carcinoid tumors was also reported Do you mean, “An increased incidence of patients with pernicious anemia later developed gastric carcinoid tumors than expected from the general population.”?

5. 3rd paragraph
   - What is the reference for your first statement that “…B12 may accelerate cancer cell proliferation…” {6)?
   - Awkward: “in such patients…return to normal” The dysplasia resolves simply by the correction of the B12 deficiency? Again for ease of the reader, would add: what percentage of patients had normalization and how many were sampled

C. Case presentation
1. Please provide the individual scores for the GS 5, e.g. 3+2?

2. “over the next 10 months….revealed rapidly progressively disease.” Would add…with an increase in his PSA to X and a decrease in his PSADT to Y.

3. What was the “clinical progression?” outside of increased PSA and upstaging based on repeat biopsy?

4. What was his baseline hgb before the “incidental diagnosis”, ie, what was it at his diagnosis of GS 5 disease which per your report would be around 10 months before the anemia diagnosis?

5. “Blocking antibody to IF was present.” For the non-hematologist like this reviewer, clarify that this means that the presentation was consistent with classic pernicious anemia.

6. Third paragraph, again, think the term “associated” is too strong an implication. What is the standard error for PSA in the lab used?
7. Please add a followup PSA after the 22.7—did the trajectory continue?

D. Conclusions

1. Please clarify this sentence: “Histologic progression is generally limited to one higher Gleason’s grade.” Do you mean that progression in this lower risk cohort is generally by a median/mean of 1 point. Irregardless, I don’t the change of 2pts is that dramatic as there can definitely be interreader variability/sampling error with GS assessment.

2. First sentence, last paragraph: “It is recommended…” Who recommends this, the authors? I think that it is a strong statement based on 1 case report. It may be more reasonable to get baseline levels in patients who have evidence of macrocytic anemia at diagnosis of PC who then pursue watchful waiting.

3. Is there a need to list Abbott’s method of measuring B12? Seems a little like an advertisement, but if not, please cite why.

E. Table

1. Would put dates at the top with descriptors (e.g., diagnosis, progression, etc) at the top
2. Please add a followup PSA as above.

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

Declaration of competing interests:

None