Reviewer’s report

Title: A word of caution: Do not wake sleeping dogs. Micrometastases of melanoma suddenly grew after progesterone treatment.

Version: 2 Date: 21 January 2013

Reviewer: Mark B Faries

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The authors present a case study of a patient treated with active, specific immunotherapy for melanoma who, in the context of receiving progesterone as treatment of an ovarian cyst, developed a rapidly progressive recurrence of disease. They review literature supporting the role of progesterone in immunomodulation and potentially melanoma progression.

Since single case reports are difficult to use as evidence of a causal relationship, some supportive correlative data would bolster this presentation. Were there any correlative findings in this patient that suggested immune suppression related to the progesterone treatment? For example, were there changes in antibody titers, delayed-type hypersensitivity testing to vaccine cells or PPD that could support the suggestion that the progesterone led to loss of immune protection and release of tumor growth?

The Journal’s guidelines suggest case reports should be based on as many as possible of the following:

1) Time relationship between intervention and reaction. With regard to this, the patient’s LDH was 309 in August 2011. What is the normal range in that institution? In our hospital that value would be considered elevated, suggesting the recurrence started before the progesterone injections.

2) Dose response relationship: this is not possible in this case as the response (disease recurrence) is a yes/no variable.

3) Supportive evidence from previous reports. The literature presents a mixed picture on this, and no clear relationship of progesterone and melanoma progression. No prior similar reports are cited.

4) Biological rationale: This is presented with the author’s discussion of the evidence for immunomodulation related to progesterone.

Overall, although this is an interesting report, it is very difficult to draw conclusions or make treatment recommendations based upon this experience.

Level of interest: An article of limited interest

Quality of written English: Acceptable
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