Reviewer's report

Title: Efficacy of T-DM1 for leptomeningeal and brain metastases in a HER2 positive metastatic breast cancer patient: new directions for systemic therapy. A case report and literature review

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Reviewer: Susan McGovern

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1. In Background, trastuzumab does not alter the natural course of breast cancer; it alters the course of the disease after treatment. "Natural course" implies the course of the untreated disease.

2. In Background, it is not true that there are "no specific treatment options" for brain metastases because SRS is a specific treatment option for brain metastases. It may be true that there are no targeted systemic options for brain metastases from breast cancer.

3. In Background, "against" in line 51 should be "compared to"

4. In Case Presentation first page, line 22, Mib-1 should be MIB-1

5. In Case Presentation second page, when the patient was staged for leptomeningeal disease, did she have an MR spine? Did she have CSF analysis? If so, what did these studies show?

6. In the Case Presentation, clarify the radiation fractionation and technique-- 30 Gy in 10 fractions? Was some technique used to minimize dose heterogeneity?

7. From the images provided, the cribiform plate and posterior orbits do not appear to have been covered by the radiation fields; these areas would be at risk in a patient with leptomeningeal dissemination. If the cribiform plate and posterior orbits were not
intentionally covered, was this decision based on the concurrent use of T-DM1, the local WBRT practice, a negative CSF result, or some other clinical factor?

8. Figure 4 and 5 could be combined. Would be nice to show a similar slice of the brain MRI at early and later follow up, instead of a slice through the optic chiasm at an early time point and a slice through the inferior cerebellum at a later time point.

9. Figure 6 restates what is in the text and could be deleted.

10. Discussion might benefit from further elaboration of the results from references #45 and #46 and a comparison of those patients with the current patient. Some of the patients in reference #46 received WBRT, but none of those patients had leptomeningeal dissemination, which should be emphasized.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript
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