Reviewer's report

Title: Brain metastasis from hepatocellular carcinoma: the role of surgery as a prognostic factor

Version: 3 Date: 2 October 2013

Reviewer: Lindsay Lipinski

Reviewer's report:

MAJOR

1. The major assumption of the article is that surgery LEADS to prolonged survival in these patients. Even though the data demonstrates improved outcomes in this patient population, only CORRELATIONS can be drawn, NOT causation. The implication that patients do better after surgical intervention can be suggested, but can certainly not be the major conclusion of the article as there is certainly not strong enough data to support such. I would therefore alter the last sentence in the conclusion, and the phrase "was shown to lead to" in the results section.

DISCRETIONARY

2. I would suggest careful use of the group of patients treated with steroids alone. This group serves really as a control/natural history of metastatic HCC, as steroids alone is a palliative measure and not really a "treatment modality."

3. It is very likely that patients who are selected for surgical resection have overall better prognoses than those who are not selected for surgery. While I would expect multivariate analysis to demonstrate this, in this case series it did not. However, I would suggest at least mentioning this in your discussion- that patients who do better after surgical resection are likely the group of patients who had either 1) disease in a less eloquent area or 2) were selected for surgery because they had better overall prognostic factors or health status. This would confound the results in terms of intervention effect vs patient selection effect.

4. I would also mention as a limitation that this data gives us no information on quality of survival, merely quantity. If patients who undergo surgical resection survive longer, but spend that time in the hospital instead of with family, then it may not be deemed a worthwhile intervention. Additionally, practically speaking, some institutions may not offer neurosurgical intervention given the overall dismal prognosis of the disease.

5. Consider including a more concise summary statement in the conclusion stating that obvious factors are positive prognostic indicators, such as younger age, better Child-Pugh, absence of intratumoral hemorrhage, but others less easy to explain, such as length of time from diagnosis. Include that patients who underwent surgical resection had better survival, and propose why this may be-
due to pathophysiology? Are patients succumbing to CNS disease? Or is this a result of patient selection?

6. What is the cause of death in these patients? CNS disease progression? Systemic progression?

MINOR
7. The use of "mental changes" should be changed to "mental status changes" or "changes of level of consciousness."

8. Define RPA class
9. Methods section- fulfills misspelled
10. Would avoid the term "aggressive" and use "surgical resection."
11. Table 1 "cerebellaR".

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: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests.