Author's response to reviews

Title: Leptomeningeal metastasis from hepatocellular carcinoma with other unusual metastases: a case report

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Author's response to reviews: see over
April 18, 2014

Dr. Yasunaru Sakuma
Associate editor, *BMC Cancer*

Re: Manuscript “Leptomeningeal metastasis from hepatocellular carcinoma with other unusual metastases: a case report”. (MS: 4967101741197004)

Dear Dr. Sakuma,

Thank you for giving us the opportunity to revise the above manuscript. We appreciate the comments and suggestions of the editor and reviewer, which were valuable in improving the quality of our manuscript. We have made extensive modifications to the original manuscript in accordance with the reviewers’ suggestions. Please find attached the revised manuscript in which major changes have been emphasized by red font for easy review. A list of responses to every question from the reviewers is also enclosed. We hope that the revised manuscript is acceptable for publication.

This revised manuscript has been edited and proofread by Medjaden Bioscience.

I anticipate hearing from you soon.

With best wishes,
Yours sincerely,

Lihua Dong

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We would like to express our sincere gratitude to the reviewers for their constructive and positive comments.

Replies to Reviewer 1
Remove the statement that WBI and effective for this disease as there is no evidence to base this on.
Response: Thank you for your insightful suggestion. This statement has been removed from the Discussion of the revised manuscript

Replies to Reviewer 2
The authors present a single case of a patient with leptomeningial metastases from hepatocellular carcinoma. In this case, only the CSF cytology finding reveal the HCC, even if the MRI finding has no typical meningeal changes. Considering from the result of CSF, it is well understand about the potential risk of leptomeningial metastases, but the brain metastases which authors described in their manuscript look likely invading to the brain ventricle. Anatomically, there is also another chance to result in CSF positive in this case. They describe this as a "very rare" case. However, to prove this situation is very difficult without autopsy in this case.
Response: Thank you for your positive comment on the present study and insightful suggestion regarding further investigation. We agree with the reviewer that tumors may invade the brain ventricle, resulting in LM. Direct spread from metastases located in the brain parenchyma that is in close opposition to the CSF space has been described previously. These tumors appear to breach the subarachnoid or ventricular spaces and diffuse widely in the CSF, although a peritumoral fibrotic reaction at the site of invasion often circumscribes this type of metastasis [1].

In this case, the patient had severe and diverse symptoms associated with the central nervous system which are the typical clinical signs and symptoms of LM, indicating that tumor cells in the CSF affect the central nervous system. As mentioned in the MS, the most common and definitive method for LM diagnosis is the demonstration of malignant cells in the CSF, or spinal MRI. CSF cytological analysis is the gold standard for identification. In this case, cytological examination of CSF was performed via liquid-based technology and the tumor cells were found in the CSF, confirming the diagnosis of LM. As the reviewer suggested, if an autopsy is performed, we may definitely prove this case.

Here we provide an additional MRI scan of the head, showing lesions in the right side of the cerebellopontine angle, indicating cranial nerve injury. This case has no specific imaging of LM such as thickness of the leptomeningeal, but has characteristic imaging including brain metastases and metastasis nodules near to the pallium, which can assist the diagnosis.

We recognize that the evidence is not sufficient to support our conclusion, however, to the best of our knowledge, this indeed was a rare case of LM from HCC.

Reference
Supplemental figure:

MRI of LM shows the lesions in the right side of the cerebellopontine angle.