Author’s response to reviews

Title: Simultaneous primary cancer occurrence of melanoma and pulmonary adenocarcinoma in leptomeningeal metastases: A case report

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Author’s response to reviews:

Resubmission letter concerning our manuscript “Simultaneous leptomeningeal metastasis from both melanoma and pulmonary adenocarcinoma – a case report?” (Manuscript ID BCAN-D-19-00752)

Dear Dr. Gummlich:

Thank you very much for providing us with the review results for our manuscript mentioned above.
We have revised the manuscript in response to the reviewers’ comments as outlined in the attached pages.

We thank the Editor and the Reviewers for their very constructive and thoughtful comments and hope that the manuscript in its revised version is now suitable for publication in BMC Cancer.

Sincerely,

Prof. Dr. Martin Glas
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Editor Comments:

“1. Please move the Declarations to just above the References. The Declarations should be in this order:
Ethics approval and consent to participate
Consent for publication
Availability of data and material
Competing interests
Funding
Authors' contributions
Acknowledgements”
Response: Changes have been made accordingly.

“2. Please clarify in the Consent for publication whether the consent was written or verbal. If verbal, why was this method chosen and was this approved by any ethics committee.”
Response: Consent for publication was written and approved by the local ethics committee.

“3. The individual contributions of ALL authors to the manuscript should be specified in the Authors’ Contributions section. Guidance and criteria for authorship can be found here:
http://www.biomedcentral.com/submissions/editorial-policies#authorship
Currently, Martin Stuschke appears to be missing from the Authors' Contributions.”
Response: We apologize for this, Martin Stuschke’s contributions have now been added.

“4. Please move the Abbreviations to come just above the Declarations (see point 1 above).”
Response: Changes have been made accordingly.
“5. Please combine the Discussion and Conclusions sections into one section entitled "Discussion and Conclusions".”
Response: Changes have been made accordingly.

Reviewer #1:

“This is a case report of a patient with leptomeningeal metastases, as stated by the authors, from both melanoma and pulmonary adenoma.

1. I doubt whether there are really leptomeningeal metastases from melanoma, as the melanoma was a pT1aN0M0 stage Clark level IV tumor, that was excised completely 9 years before the leptomeningeal metastases occurred, without any systemic metastases from melanoma.

The only reason to conclude that there are LM from malignant melanoma are the HMB45 and MelanA positive cells in CSF, as NSCLC can also be BRAF positive (<5%).

Looking at figure 1B and 1D, could these HMB45 and MelanA positive cells not just be cells of the immune system (monocytes/macrophages)? Is the cytopathology of cells in figure 1B and 1D not compatible with cells of the immune system?

And could there be cross-reactivity of this MelanA and HMB45 staining, leading to an erroneous conclusion that these are melanoma cells? Or couldn't this be just melanocytes instead of malignant melanoma cells?”

Response: We thank the reviewer for this critical and essential remark. By the cytomorphological appearance, we are confident that these cells do not stem from the immune system (or are non-malignant cells) for the presence of tumor-specific hallmarks: enlarged nucleus, shifted nucleus-cytoplasmin ratio, nuclear morphology. While MelanA was discovered as an antigen recognized by cytotoxic T-cells 1, a corresponding tumor-specific cytomorphological presentation precludes the presence of immune cells in the case at hand. In addition, the co-occurrence of the melanocytic marker HMB45 (which is not found in non-tumor cells, except for melanocytes) makes immune cells even less probable. Melanocytes may express both MelanA and HMB452, the cytomorphologic presentation, however, argues against melanocytes and favors melanoma cells. In conclusion, the presented findings can best be reconciled with metastatic melanoma. We have taken up this interesting comment and incorporated it into the text (discussion part). We hope that we could address this issue to the reviewer’s satisfaction.

2. The resolution of the MRIs is not sufficient enough. The presence of leptomeningeal contrast enhancement on this MRIs (and the response of therapy) cannot be determined based on these pictures. Please provide MRI scans with a higher resolution.
Response: We have replaced the MRI images by better resolution ones.

Reviewer #2:

“There are only minor suggested changes. Lines 105 and 185 the authors use the term releasing the breaks on precision medicine. I suggest that they replace this with "thereby facilitating" personal medicine.
Line 161: should read: "DNA analysis revealed the presence of wildtype B-Raf, mutant TP53, and mutant KRAS genes as detected by next-generation sequencing.”
Response: We thank the reviewer for the suggestions, which are now implemented accordingly.

References:
