Dear Editor

We would like to thank the editors and reviewers for their helpful comments and suggestions for improving our manuscript. Our point-by-point responses to the editors' and reviewers' comments are presented below.

Reviewer #1

1) "Signed Informed Consent Form(s) or Document(s)" did not meet the standard of the published informed consent form for publication.

Response: Thank you for the suggestion. The informed consent has been amended and uploaded.

2) "CASE SUMMARY" did not provide sufficient details of clinical descriptions.

Response: Thanks for your important comment.We made a detailed summary of this case from the aspects of the patient's chief complaint, medical history, physical signs, examination, treatment and recovery according to your valuable suggestions.（**Line 9 - 22/page3** ）

3) "Core tip" should be specific about this report, not the generic introduction of GBM.

Response: Thank you for the suggestion.We have summarized the novel points and key points of the case according to your suggestions. Please refer to the article for details.（**Line 8- 11/page4** ）

4) At first MRI and pathology of diagnostics, any survey on other organs (e.g., the skull, scalp, ribs, spine, liver, and lungs)? It seems they did not check other organs except the brain by the following: that "Laboratory examinations Blood analysis revealed mild leukocytosis 12.5 × 109/L, with predominant neutrophils (80%) with normal hematocrit and platelet count. Other tests were within the normal range. Imaging examinations Magnetic resonance imaging (MRI) of the brain revealed a space-occupying lesion in the right temporoparietal occipital region (Figure 1A). Chest computed tomography (CT) and abdominal ultrasound were negative. Further diagnostic work-up After admission, the lesion was extensively excised, and the ventricle was opened intraoperatively (Figure 1B). Pathological examination revealed that immune phenotype IDH1 wild type, IDH2 wild type, MGMT unmethylated, and the diagnosis was glioblastoma (World Health Organization grade IV) (Figure 1C–1E)." Only did they check "Six months after surgery, the patient had a mass at the site of the surgical incision (Figure 2A), and intracranial recurrence and subcutaneous metastasis were considered in the re-examination of enhanced MRI (Figure 2B)."

Response: Thank you for the suggestion.In addition to the preoperative head MRI examination, the patient also received routine preoperative examinations such as head CT, chest CT and abdominal ultrasound. Head CT and MRI showed no abnormalities of skull and scalp, chest CT showed no abnormalities of spine, ribs and lung, and abdominal ultrasound showed no liver mass. Therefore, the systemic multi-organ tumor after surgery was considered to be caused by GBM extracranial multi-organ metastasis.（**Line 22-23/page5** ）

5) They did not discuss any treatment-driven changes (doi: 10.1158/0008-5472.CAN-19-2452) (doi: 10.1007/s11060-020-03598-2) (doi:

10.1200/JCO.19.00367)

Response: Thank you for the suggestion.We have made modifications according to your suggestions in the discussion section（**Line 14-22 /page9**）.

6) Fig 1 C, D, E should be marked with scale bars, while A and B should be marked with arrows. The rule must be applied to all other figures. “C) Hematoxylin and eosin staining of the excised temporal lobe of the patient’s head suggested glioblastoma” – this was not a sufficient description of pathology reports.

Response: Thank you for your advice. We have arrows for all the imaging examinations and have scaled all the pathological images. In addition, Hematoxylin and eosin staining were described in detail according to your valuable suggestions. (Image at 200 × magnification).

7) Fig 3 should be presented with pathology supporting figures.

Response: Thank you for the suggestion. First of all, based on the pathological results of the patient after the second surgery and cervical lymph node pathology, we considered that the mass in the patient's spine and ribs was caused by extracranial metastasis of glioblastoma. We conducted a systemic assessment of the patient and listened to the opinions of his family members before palliative treatment. In addition, we invited two neuroimaging experts and a veteran neurosurgeon to guide the case, and they all agreed that the patient was a glioblastoma with extracranial multiple organ metastasis. Therefore, we do not have relevant pathological images in Fig3, but according to relevant impact results and expert guidance, GBM extracranial multiple organ metastasis was considered in this case.

Reviewer #2

1. Delete seperate dot after whole paragraph of conclusion part of Abstract (page 3).

Response: Thanks for your reminding. We have revised the article according to your suggestions.

2. Correct few excessive spaces e.g. in Author contributions section or "skull, scalp" in Outcome and Follow-up section.

Response: Thank you for your suggestion. We have revised it and checked it in detail.

3. Although "CNS" abbreviation is well known, please explain it at first use.

Response: Thank you for the suggestion. CNS is central nervous system.We have made corresponding supplement in the article, thank you.（**Line 15/page7** ）

4. At least one "so" word in the Conclusion section could be changed to "thus"..

Response: Thank you for the suggestion. We changed the second "so" to "thus"(**Line 6 in conclusion**).

5. Please consider improvement of Table 1 in terms of columns' width to ease readbility of some words.

Response: Thank you for your suggestion. We have made appropriate changes to the form.

6. Begin with upper case for figure's description ("images" of Figure 1)

Response: Thanks for your reminding, we have made corresponding modifications.

7. Although there are scale bars in all required subfigures, is this possible to mention about its length in figure's description? I can see the bar but not the value itself.

Response: Thanks for your reminding, we have made corresponding modifications.Each pathological image was marked with the corresponding scale and the corresponding lesion site.

8. The sentence of Introduction i.e. "We report a case of postoperative glioblastoma with not only extracranial metastasis but also multiorgan metastasis and review the relevant literature" could be changed to "We report a case of postoperative glioblastoma with not only extracranial metastasis but also multiorgan metastasis; the relevant literature is subsequently reviewed."

Response: Thank you for your guidance. We have made corresponding modifications.（**Line 16- 18/page4** ）

9. In section Final diagnosis, you can consider adding "IDH wild-type" after glioblastoma for full view on clinical case. I am aware that in previous section (Further diagnostic work-up) you mentioned about IDH1/2 wild type but still I believe that it is appropriate to specify which glioblastoma, as this is "Final diagnosis". Please refer to doi: 10.1007/s00401-016-1545-1.

Response: Thanks for your important comment.We referred to the latest WHO diagnostic criteria in 2021, doi: 10.1093/neuonc/noab106.（**Line 7/ page6** ）

10. Lastly, the submitted document has 17 pages but the information in the bottom corner shows [page number]/18. Is this possible that something is missing? I suspect not, as the submission and main text refers to all figures/tables which are provided, but want to notify you just in case.

Response: Thank you for your attention. The article submitted before only has 17 pages, and the extra pages will be deleted in time. I'm very sorry.

Best wishes,

Xingzhao Luan, on behalf of all coauthors.
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