

Dear editor,

Thank you for giving us the opportunity to re-submit a revised version of our manuscript titled “A Case of Skeletal Muscle Metastases of Hepatocellular Carcinoma” to the World Journal of Clinical Cases. The manuscript ID is 59596.

We appreciate the time and effort that you and the reviewers have dedicated to providing your valuable feedback on our manuscript. We are grateful to the reviewers for their insightful comments and suggestions on our paper.

We have provided a point-by-point response to each reviewer’s comment following this cover letter. We hope that you find our responses satisfactory and that the revised manuscript is now suitable for publication in the World Journal of Clinical Cases.

We look forward to hearing from you in due time regarding our submission and to respond to any further questions and comments you may have.

Sincerely,

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Reviewer 1

Thank you so much for your very interesting case report. Overall, this seems to be one of the first reported cases of Hepatocellular Carcinoma with metastasis to the skeletal muscle. This case report has a number of strengths, but there are areas for improvement prior to acceptance. Overall, there are grammatical errors that need to be corrected and a better timeline needs to be established.

Response: The authors would like to thank the reviewer very much for the suggestion. We have revised the manuscript, including the correction of grammatical errors.

(1) The same sentences from the introduction are copied into the discussion, specifically the first paragraph and a large portion of the second paragraph of the Discussion is taken verbatim from the Introduction or elsewhere in the report

Response: The authors would like to thank the reviewer very much for the suggestion. Thank you for your valuable suggestions. We have made corresponding adjustments.

(2) There are a number of grammatical errors throughout the article that require correction. Minor concerns: The original details of the primary cancer (HCC) need to be described given the rarity of this finding, specifically the initial stage, if there was vascular invasion and other such details.

Response: The authors would like to thank the reviewer very much for the suggestion. We have corrected the grammatical errors. The patient underwent liver transplantation due to primary liver cancer as I mentioned in the revised manuscript.

(3) Title: The title is not clear. The use of the descriptor “long term” is potentially confusing to the readers. In addition, it might be more specific to say hepatocellular carcinoma as opposed to liver cancer

Response: The authors would like to thank the reviewer very much for the suggestion.

The title has been modified as ‘A Case of Skeletal Muscle Metastases of Hepatocellular Carcinoma’.

(4) Keywords: The keywords could be more focused on the specific case instead of broad topics such as “ultrasound” and “pathological.” These can frequently be found among Medical Subject Headings in PubMed.

Response: The authors would like to thank the reviewer very much for the suggestion. Hepatocellular carcinoma (HCC); Transplant; Skeletal muscle metastasis (SMM); Pathological; Case report.

(5) Abstract: Please provide tumor type and not “liver tumor.”

Response: The authors would like to thank the reviewer very much for the suggestion. We have modified as suggested primary liver cancer.

(6) Core tip: "Skeletal muscle delivered factors may play a vital role in the rarity of skeletal muscle metastasis. Therefore further studies should be carried out to estimate the biochemical characteristics of skeletal muscle delivered factors and their anti-tumor activity". This appears somewhat inappropriate as a summary of a case report. It is unclear what “skeletal muscle delivered factors” are. Introduction: The referencing is commended, but there are unsupported statements in the manuscript. For example, the first line of your Introduction – “Hepatocellular carcinoma (HCC) is ranked sixth in malignancies and fourth in the mortality rate.” would benefit from a source and this

exact sentence is repeated in the Discussion. In addition, re-wording would assist this statement.

Response: The authors would like to thank the reviewer very much for the suggestion. As suggested by the reviewer, we have modified the sentences in Core tip and Introduction and included references.

(7) Introduction: When discussing the skeletal muscle metastases, it would be more clear if you defined this as “Metastases to the skeletal muscle from HCC.” Also, it would be beneficial to discuss the most common sites of HCC metastasis in your introduction.

Response: I couldn't agree with you more,thank you for your suggestions and I have added “Extrahepatic HCC can occur in 1 of 3 ways: direct extension, hematogenous spread, or lymphatic invasion. Rupture of a HCC focus may result in intraperitoneal implantation of tumour cells onto peritoneal or omental surfaces. Reported frequencies of HCC metastatic sites include lungs, lymph nodes, bone, and brain. Rare sites of metastasis include the rectum, spleen, diaphragm, duodenum, esophagus, pancreas, seminal vesicle, and bladder”.

(8) Be sure to accurately label imaging and be careful with phrases such as “Arterial spectrum.”

Response: The authors would like to thank the reviewer very much for the suggestion. We have replaced “Arterial spectrum.” to ” Power Doppler activity revealed significant increased flow within the tumor”.

(9) Provide clarification on phrases such as “Spindle mass” (page 5, line 83).

Response: The authors would like to thank the reviewer very much for the suggestion. We have replaced it with ‘circumscribed mass’.

(10) Figure 3: be more specific about what the IHC stains are indicating.

Response: The authors would like to thank the reviewer very much for the suggestion. We have included Hematoxylin stain X20.

(11) Discussion: It is recommended to avoid generalized statements such as “and so on” – page 9, line 148, “etc” on page 9, line 160.

Response: The authors would like to thank the reviewer very much for the suggestion. As suggested, We have deleted it.

(12) Discussion: The discussion should focus on a relevance to the case. You describe three types of MRI findings on line 155 of page 9, but significance to the case is not provided. Also, the differential diagnosis discussion could be shortened and more focused.

Response: The authors would like to thank the reviewer very much for the suggestion. As suggested, we have removed the irrelevant portion.

(13) Conclusion: In the conclusion, it is mentioned that skeletal muscle metastases have a poor prognosis, but there are no statistics/references presented to support that statement.

Response: The authors would like to thank the reviewer very much for the suggestion. We have explained it and added references “Skeletal muscle metastases have a poor

prognosis, which could cause functional impairment and increasing short-term postoperative morbidity in patients both with and without malignant diseases”.

(14) Conclusion: Clarify the timing of the resection versus when this case report was written. You state he is in “good condition” but how long post op is the patient. Also, clarify whether any chemotherapy or additional therapy was required.

Response: The authors would like to thank the reviewer very much for the suggestion. I rearranged the language and The patient was not given chemical or radiation therapy.

(15) Conclusion: Clarify what you mean by “Due to a lack of data, we have not been able to draw a firm conclusion.” It is not clear what that conclusion is focused on.

Response: The authors would like to thank the reviewer very much for the suggestion. We abridged the sentence in order to make the article easier to understand.

(16) Referencing: References are not provided in numerical order.

Response: The authors would like to thank the reviewer very much for the suggestion. The order of references has been reorganized in the revised form.

Reviewer 2

An interesting case report on a very rare presentation of metastatic liver tumour. Exceedingly rare, especially 6 years after a transplanted liver for liver cancer. The manuscript is well written and the relevant question as to the possible mechanism for this is asked. The language needs minor revision. I have enclosed some suggestions as attachment

Response: The authors would like to thank the reviewer very much for the suggestion.

We have made modified the sentences.

Reviewer 3

The article needs a better literature review in the field of skeletal muscle metastases.

Response: The authors would like to thank the reviewer very much for the suggestion. As suggested, we have revised the case discussion section to make it more complete and added more literature.

LANGUAGE QUALITY

Please resolve all language issues in the manuscript based on the peer review report. Please be sure to have a native-English speaker edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability, so that the manuscript's language will meet our direct publishing needs.

Response: The authors would like to thank the reviewer very much for the suggestion. We have been invited a native-English speaker to edit the manuscript and made the modifications, and we hope that the revised manuscript will meet your publishing requirements.

EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

1 Scientific quality: The manuscript describes a case report of the long-term skeletal muscle metastases of liver cancer. The topic is within the scope of the WJCC. (1)

Classification: Grade B and Grade D; (2) Summary of the Peer-Review Report: The authors reported an interesting case report on a very rare presentation of metastatic liver tumour, which is exceedingly rare. The manuscript is well written and the relevant question as to the possible mechanism for this is asked. However, the language needs minor revision. A better literature review should be added; and (3) Format: There are 3 figures. A total of 30 references are cited, including 11 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Grade B and Grade B. 3 Academic norms and rules: The authors provided the CARE Checklist–2016, and Written informed consent. The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the CrossCheck detection and Bing search.4 Supplementary comments: This is an unsolicited manuscript. The topic has not previously been published in the WJCC.

Response: Thank you for your suggestions. We have revised the language and added literature to make it better and provided the signed conflict-of-interest disclosure form and copyright license agreement.

5 Issues raised: (1) The “Author Contributions” section is missing. Please provide the author contributions;

Response: We have been added “Author Contributions” in this article.

(2)The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Response: The authors would like to thank the reviewer very much for the suggestion. The original pictures have now been put into the PPT format according to your requirements.

(3) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

Response: We have provided the PubMed numbers and DOI citation numbers to the reference list, including a list authors of the references. We have to note that reference 23 and 27 has no DOI number, so DOI number of reference 23 and 27 could not be added in the revised manuscript.

(4) The “Case Presentation” section was not written according to the Guidelines for Manuscript Preparation. Please re-write the “Case Presentation” section, and add the “FINAL DIAGNOSIS”, “TREATMENT”, and “OUTCOME AND FOLLOW-UP” sections to the main text, according to the Guidelines and Requirements for Manuscript Revision.

Response: According to the Guidelines for Manuscript Preparation. we have re-written the “Case Presentation” section and added the “FINAL DIAGNOSIS”, “TREATMENT”, and “OUTCOME AND FOLLOW-UP” sections to the main text.