

October 1, 2022

Li Ma

Science Editor, Editorial Office Director, Company Editor-in-Chief, Editorial Office

World Journal of Gastrointestinal Oncology

Dear Editor:

We would like to thank you for the opportunity to revise and resubmit our manuscript, entitled "*A massive, rare tumor: hepatic hemangioblastoma.*" The manuscript ID is 79634. The manuscript has been carefully rechecked and appropriate changes have been made in accordance with the reviewers' suggestions. The responses to their comments have been prepared and attached herewith. We thank you and the reviewers for your thoughtful suggestions and insights. This manuscript has benefited from these insightful suggestions. We look forward to working with you and the reviewers to bring this manuscript closer to publication in the *World Journal of Gastrointestinal Oncology*. Please let us know if you have any concerns about the manuscript. We would be happy to address them as soon as possible. Thank you for your consideration. I look forward to hearing from you.

Sincerely,

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Reviewer #1:

1. Please rewrite the paper's title to better explain the study's purpose.

Response: Thank you for the careful review and pertinent comments and recommendations. We have rewritten the title, accordingly (Page 1, line 4).

2. The phrase "literature review" should be removed from the paper's title.

Response: The term "literature review" has been removed from the title of the paper, accordingly.

3. Rewrite the study abstract in a concise and attractive manner.

Response: The study abstract has been rewritten (Page 2).

4. The study's objective should be stated in the final paragraph of the introduction.

Response: The purpose of the study has been stated in the last paragraph of the introduction (Page 3, lines 12 and 13).

5. Considering the use of modern references beginning at least in 2015, with any references after this year being replaced with newer references.

Response: Three references on hepatic hemangioblastoma could not be updated, most of the remaining references have been updated 2015 or more recent.

6. Make the final paragraph of the discussion focus on the current case study's limitations, strengths, and future directions in medical imaging findings of hepatic hemangioblastoma.

Response: The limitations, strengths, and future directions of medical imaging findings for hepatic angiogenic cell tumors of the current case study have been described in the final paragraph of the discussion as requested (Page 8, lines 14-22).

7. Rewrite the conclusion section once more.

Response: The conclusion section has been rewritten (Page 8, lines 24-27, and page 9, lines 1-3).

8. Some typos must be corrected. best wishes.

Thank you for your recommendation. The manuscript has been checked by a professional, native English-speaking researcher.

Reviewer #2:

1. Specific Comments to Authors: Expand introduction (see file) Hemangioblastomas are rare benign tumors, accounting for 1–2% of all central nervous system tumors[1,2]. The cerebellum is the most common location, followed by the spinal cord and brainstem[3], but hemangioblastomas can also occur in the peripheral nervous system, adrenal gland, and liver[4]. Hemangioblastomas are present in 25–30% of patients with von Hippel–Lindau disease (VHLD), and in these cases, retinal hemangioblastomas and endolymphatic sac tumors may also be detected [4]. Mourão JLV, Borella LFM, Duarte JA, et al. Imaging manifestations of von Hippel-Lindau disease: an illustrated guide focusing on the central nervous system. Radiol Bras. 2022;55:188–92. Imaging findings What about diffusion weighted images?

Response: Thank you for the careful review and pertinent comments and recommendations. Accordingly, the discussion section has been rewritten in to describe diffusion-weighted images (Page 7, lines 12-20).

2. Typically, hemangioblastomas facilitate diffusion. There were flow voids on T2 weighted images? Please, expand the description.

Response: In paragraph 2 of the discussion, we have described the blood flow voids on T2WI images (Page 7, lines 8-11).

3.What was the first diagnosis considered?

Response: After multi-disciplinary team consultation, considering hepatic mesenchymal tumors, atypical hemangioma or solitary fibrous tumor was determined to be likely (Page 4, line 24, and page 5, line 1).

4. Did you use gadoxetic acid-enhanced MRI? It is widely used to detect and characterize various hepatic nodules. The high contrast generated by gadoxetic acid between focal hepatic lesions and the background parenchyma in the

hepatobiliary phase (HBP) helps in differentiating early HCC from benign nodules.

Response: China has a high incidence of liver cancer. Therefore, Gadoxetic acid-enhanced MRI was widely used, especially for patients with hepatitis B and liver cirrhosis. However, this tumor was too large and the patient did not have a history of hepatitis B or cirrhosis. Further, plus this medication requires out-of-pocket payment in our unit, so we chose only Gadoteric acid meglumine according to the patient's needs.

5. In discussion: Spinal cord? Retina? Abdominal visceral involvement of VHL usually includes simple hepatic, renal, and pancreatic cysts or tumors of the kidney or pancreas and pheochromocytoma. Details of the contrast used in the discussion.

Response: Thank you for your query. Yes, VHL involves numerous sites and is mostly combined with simple liver, kidney, or pancreatic cysts or kidney or pancreatic tumors and pheochromocytomas. Our case was probably a sporadic hepatic hemangioblastoma, therefore, we did not observe much involvement of VHL-related lesions in areas other than the liver.

6. Hepatic lesions in VHL have been previously reported as adenoma, and hemangioma. What was your preoperative diagnosis of the case? It is interesting to discuss...?

Response: Thank you for your query.

Imaging findings: the tumor was massive, with expansive growth and well-defined boundaries, and there was no invasion of adjacent hepatic vessels or breakthrough of the hepatic capsule. There were no emboli in the portal vein or enlarged lymph nodes in the hepatic portal or retroperitoneum. Contrast-enhanced scans showed heterogeneous mild progressive enhancement. On physical examination, the abdomen was flat and a hard mass was palpable under the hepatic rib cage. and denied any history of infectious diseases, such as "hepatitis or tuberculosis."

A multi-disciplinary team consultation, It is considered as a benign tumor with mesenchymal tissue source, concluded that atypical hemangioma or solitary fibrous tumor was likely.

7. What lessons did you have with the case? It is important to emphasize.

Response: We carefully compared the features of this case with those of the lesions of the previous three cases and found that some features were similar. For example, the patient was between 30-45 years old when the lesion was found, the tumors were large in size, all were predominantly solid with heterogeneous density, and were seen mostly in the right lobe of the liver, with obvious blood supply vessels visible on either angiography or MR, and all were progressively enhancing after enhancement. In addition to the fact that this case may be sporadic rather than VHLD-related.

we found some other differences from the previous three cases. For example, in this case, the hemangioblastoma occurred only in the liver, but not in other areas. The degree of enhancement in this case was less than that in the previous three cases. Although the enhancement was progressive, this case did not show an outward-to-inward filling pattern. Therefore, to summarize these characteristics of hepatic hemangioblastoma.

we have some experience.1. Hepatic hemangioblastoma is rare and not easily diagnosed in clinical work.2. Tumors are mostly seen in young and middle-aged people, and there is no significant difference between men and women.3. Clinical symptoms are variable, but most of them may be related to VHLD.4. Tumor enhancement is progressive.5. There are obvious thick blood supply vessels.6. MR or CT enhancement scan can detect blood supply vessels instead of angiography.7. MR or CT scan can replace angiography to detect blood supply vessels, thus reducing unnecessary invasive examinations.7. Hepatic hemangioblastoma is mostly solid, distributed in the right lobe of the liver, and the tumor is mostly huge when found.

8. Please include a table with characteristics of all reported hepatic hemangioblastomas in the literature.

Response: Thank you for your recommendation. A table of the characteristics of all reported hemangioblastomas in the literature has been included as requested and upload

In conclusion, add that: Other common features are the presence of flow voids on T2 WI and components which facilitate diffusion (hemangioblastoma is the only tumor that can facilitate diffusion which is a key role to the diagnosis).

Response: Thank you for your query. Additional information has been provided, as requested.

Re-reviewer

Specific comments to authors:

The authors present a case report of clinical interest, which is documented by interesting images. The subject falls within the scope of the journal. Description and discussion of the findings are well done and well-founded. The bibliography is pertinent and current. However, the text needs improvement. Excerpts that deserve special attention are marked in yellow in attach file.

Response:

1. New references have been inserted into the introduction as required, and the order of all other references has been adjusted accordingly.
2. The terms 'the left ureteral calculus with dilatation' and 'Ultrasonography revealed left ureteral calculi with dilatation.' have been revised in the text.
3. All other yellow-highlighted sections have been carefully checked; we thank you for your detailed guidance.
4. The informed consent form has been uploaded along with the revised manuscript.

4 LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

As the revision process results in changes to the content of the manuscript, language problems may exist in the revised manuscript. Thus, it is necessary to perform further language polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A).

Response: The required touch-ups have been made and the certificate of editing has been uploaded.

5 ABBREVIATIONS

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, and mAb, do not need to be defined and can be used directly.

Response: Abbreviations have been used in the text as required.

6 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:

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, the relevant ethics documents, and the English Language Certificate, all of which have met the basic publishing requirements of the Gastrointestinal Oncology, and the manuscript is conditionally accepted. I have sent the manuscript to the

author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

Response: Each figure has been organized into a single PowerPoint file as requested, and submitted on the system as "79634-Figures.pptx"

(2) Requirements for Tables: Please provide decomposable Tables (in which all components are movable and editable), organize them into a single Word file, and submit as "79634-Tables.docx" on the system. The tables should be uploaded to the file destination of "Table File".

Response: Decomposable forms of the tables have been provided as requested, organized into a Word file, and submitted in the system as "79634-Tables.docx."