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Associated Prof. Andrzej S Tarnawski, MD, PhD

Editors-in-Chief

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Dear Editors:

Thank you for providing us an opportunity to submit a revised draft of our manuscript for publication in *World Journal of Gastroenterology*, titled "Gallbladder Burkitt's lymphoma mimicking gallbladder cancer: A case report."

Your comments, as well as those of the reviewer, were highly insightful and enabled us to greatly improve the quality of our manuscript. We have amended the attached manuscript in accordance with the detailed suggestions you have graciously provided. In the following pages, I have provided our point-by-point responses to all comments and have quoted the revised portions of the manuscript. The changes in the attached revised manuscript have been indicated using underlined text.

I hope that you will find our revised manuscript suitable for publication in *World Journal of Gastroenterology*. I look forward to hearing from you at your earliest convenience.

Sincerely,

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Response to the Reviewer

Thank you for your comments on our manuscript. We sincerely appreciate these insightful comments, which have helped us greatly improve the revised manuscript. Our point-by-point responses to the comments are presented below.

Comment 1: “An 83-year-old man with no complaints had a gallbladder tumor” How was tumor diagnosed? (abstract)

Response: We thank the reviewer for this comment. We have modified the text as follows:

Page 3, lines 10-12

An 83-year-old man with no abdominal complaints was found to have a gallbladder tumor and periportal lymph node enlargement on computed tomography performed for hypertension screening.

Comment 2: “Biopsy is recommended in cases with suggestive findings of gallbladder malignant lymphoma.” There are hardly any features suggestive of gallbladder

lymphoma. Please modify the conclusion.

Response: As the reviewer pointed out, preoperative diagnosis of gallbladder malignant lymphoma is quite difficult, and almost all patients are preoperatively diagnosed as having gallbladder cancer or cholecystitis. Although some previous reports have suggested the possibility of accurate preoperative diagnosis by using imaging findings, these reports have limitations. The invasiveness of extrahepatic bile duct resection combined with hepatectomy is much greater than that of tumor biopsy, and it is conceivable that differences in intervention may be associated with the prognosis, as in this case. Hence, we would recommend biopsy in case of suspicion of previously reported characteristic images. However, as the reviewer commented, there is no doubt that preoperative diagnosis is difficult, and we have changed the description in the text as follows:

Page 4, line 1-2

Biopsy can be useful in cases with findings suggestive of gallbladder malignant lymphoma.

Page 9, lines 13-15

Therefore, this disease should be considered in the differential diagnosis of a gallbladder tumor, and biopsy can be useful in facilitating the early introduction of chemotherapy in cases with suggestive imaging findings.

Comment 3: Please write "gall bladder" as "gallbladder". (introduction)

Response: Thank you for pointing out this typo. We have corrected the relevant sentences in the revised manuscript as follows:

Page 5, lines 2-4

In almost all cases of this malignancy, patients are diagnosed as having gallbladder adenocarcinoma or cholecystitis at the time of surgery, and preoperative diagnosis is extremely difficult.

Comment 4: In almost all cases of this malignancy, patients are diagnosed as having gallbladder adenocarcinoma or cholecystitis at the time of surgery, and preoperative diagnosis is extremely difficult. Please cite a recent paper published in World J

Gastroenterol (PMID: 33177791).

Response: We thank the reviewer for this comment and recommendation of citation of the useful report. Accordingly, we have cited the report by Gupta P et al. in the revised discussion and have included the report as reference #13 in the revised reference list.

Comment 5: Case presentation Better to write as "no abdominal complaints" rather than "no complaints".

Response: Thank you for this pertinent comment. We have modified the relevant sentences in the revised manuscript as follows:

Page 5, lines 13-15

An 83-year-old man with no abdominal complaints was found to have a gallbladder tumor along with periportal lymph node enlargement and was admitted to our institution for further investigation.

Comment 6: Please replace "enhanced" with "contrast enhanced".

Response: We have made the necessary changes throughout the revised manuscript as follows:

Page 6, lines 8-11

A contrast-enhanced abdominal CT scan revealed two irregular and highly contrast-enhanced masses at the neck and body of the gallbladder as well as periportal lymph node enlargement, measuring 30 × 20 mm in diameter and consistent with gallbladder cancer lymph node metastasis (Figure 1).

Page 11, lines 2-5

Figure 1: A contrast-enhanced abdominal computed tomography scan shows two irregular and highly contrast-enhanced masses (arrowheads and arrow) at the neck and body of the gallbladder as well as periportal lymph node enlargement, which is consistent with gallbladder cancer lymph node metastasis.

Comment 7: “A contrast-enhanced abdominal CT scan revealed two irregular and

highly enhanced masses at the neck and body of the gallbladder as well as periportal lymph node enlargement, measuring 30 × 20 mm in diameter and consistent with gallbladder cancer metastasis.” This is not correct as GB metastasis is very rare and there are no characteristic findings.

Response: Thank you for providing these insights. We made this statement with the intention that the lymph node enlargement was considered a lymph node metastasis. In response to the reviewer’s comment, we have modified the relevant text in our revised manuscript as follows:

Page 6, lines 8-11

A contrast-enhanced abdominal CT scan revealed two irregular and highly contrast-enhanced masses at the neck and body of the gallbladder as well as periportal lymph node enlargement, measuring 30 × 20 mm in diameter and consistent with gallbladder cancer lymph node metastasis (Figure 1).

Page 11, lines 2-5

Figure 1: A contrast-enhanced abdominal computed tomography scan shows two irregular and highly contrast-enhanced masses (arrowheads and arrow) at the neck

and body of the gallbladder as well as periportal lymph node enlargement, which is consistent with gallbladder cancer lymph node metastasis.

Comment 8: “Furthermore, in this case, a discrepancy existed in that no serosal invasion was observed despite the size of the tumor and presence of lymphadenopathy. This might be a characteristic finding that distinguishes gallbladder malignant lymphoma from carcinoma.” Please give reference for this Legends.
(discussion)

Response: We thank the reviewer for this comment. These statements are the opinions of the authors, and hence, these have not been cited. In the revised manuscript, we have modified the sentences to make it clear that these statements are our opinion. The relevant text has been revised as follows:

Page 9, lines 6-7

We think this might be a characteristic finding that distinguishes gallbladder malignant lymphoma from carcinoma.

Comment 9: The authors state that the findings of CT are consistent with metastases.

This is not correct as GB metastasis is very rare and there are no characteristic findings. (Figure 1)

Response: We thank the reviewer for this comment. Please refer to our response to comment 7, which should address your concern.