

Manuscript revision reply to Reviewers' Comments

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 74958

Title: Complete Resection of Combined tumor (Large cell neuroendocrine carcinoma and hepatocellular carcinoma) of the Liver with Lymph Node metastasis: a rare case report

Reply to Reviewers' Comments

We are grateful to the Editors and Reviewers for meticulous examination and appropriate comments for our manuscript, which has served to ameliorate this revision. We have amended our manuscript and performed additional correction to address the Reviewers' comments and concerns. Detailed point-by-point responses are as follow,

● Reviewer #1 :

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: This manuscript reports a rare case with collision tumors consisting of large-cell neuroendocrine (90%) and hepatocellular(10%). Here are two suggestions for revising this manuscript.

1. According CARE Checklist-2016, Key Words should include four to seven words, and should include "case report" as one of the words.

> Thank you for your insightful comment. We added the above-mentioned comment in the Key words as "hepatocellular carcinoma, neuroendocrine carcinoma, chronic

hepatitis B, Case report“

2. Considering the rarity of neuroendocrine carcinoma of the liver, and PETCT is not a specific test for neuroendocrine tumors, how to explain that neuroendocrine tumors of the liver may metastasize from neuroendocrine carcinomas of other organs?

> We appreciate your meticulous comments for our manuscript. PETCT is not a specific test for neuroendocrine tumors. We added the above-mentioned comment in the Imaging examinations as “The patient refused biopsy and decisively wanted surgery. However, a routine workup was performed to check for metastasis. The chest CT and bone scan showed no metastatic lesions. 18F-fluorodeoxyglucose positron emission tomography-computed tomography (PET-CT) was performed to exclude the possibility of neuroendocrine tumors of the liver metastasizing from neuroendocrine carcinomas of other organs.”

● **Reviewer #2 :**

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This manuscript is interesting, and I recommend the acceptance after some revision.

1. This manuscript should be prepared according to the guideline of BPG publishing.

> We appreciate your thoughtful comments for our manuscript. We corrected our manuscript and figures according to GUIDELINES FOR MANUSCRIPT PREPARATION, SUBMISSION, AND MANUSCRIPT FORMAT.

2. Some information was missing, such as "The Institutional Review Board of OO

National University Hospital Clinical Trial Center approved the study (approval no. 2201-005-111)." OO refers to what? Trial may be corrected as Trail. 3. The more detailed description of Figure legend should be corrected.

> Thank you for your insightful comment. We corrected the above-mentioned comment in the Institutional review board statement as "The Institutional Review Board of Pusan National University Hospital approved the study (No. 2201-005-111) and conducted ethically in accordance with the World Medical Association Declaration of Helsinki." We corrected our figures according to BPG submission guidelines and added detailed description of Figure legend as

Figure 1. "Abdominal contrast-enhanced computed tomography (CT) examination of the collision tumor. A: Before contrast. B: Arterial phase. C: Portal venous phase. D: Delayed phases. CT images demonstrate a 4.5-cm mass (arrowhead) in S3. This mass shows peripheral rim enhancement during the arterial phase and washout during the portal venous phase and delayed phase. This mass was categorized using liver imaging reporting and data system M observations. CT images also demonstrate a 1.3-cm metastatic lymph (arrow) node along the common hepatic artery."

Figure 2. "Gadoxetic acid-enhanced liver magnetic resonance imaging. A: T2-weighted image. B: Before contrast. C: Arterial phase; D: Portal venous phase. E: Transitional phase. F: Hepatobiliary phase. Magnetic resonance (MR) images demonstrate a 4.5-cm mass (arrowhead) in S3. This mass presents subtle high signal intensity to adjacent hepatic parenchyma, peripheral rim enhancement during the arterial phase, and washout during the portal venous phase, transitional phase, and hepatobiliary phase. This mass was categorized using liver imaging reporting and data system M observations. MR images demonstrate a 1.3-cm metastatic lymph (arrow) node along the common hepatic artery."

Figure 3. "18F-fluorodeoxyglucose positron emission tomography-computed tomography examination (PET-CT). PET-CT image demonstrates a 4.5-cm hypermetabolic mass (arrowhead) in S3 and a 1.3-cm metastatic lymph with avid

FDG uptake (arrow) in the node along the common hepatic artery.”

Figure 4. “Histopathological analysis and immunohistochemical examination of the resected specimen. The collision tumor comprises two distinct components: large-cell neuroendocrine carcinoma (red arrow) and hepatocellular carcinoma (black arrow). A: Hematoxylin-eosin staining (x40). Immunohistochemical staining (B) for CD56 (x100) and (C) glutamine synthetase staining (x100). (D) Hepatocyte-specific antigen staining (x40).”

We would like express our gratitude to the *World Journal of Clinical Cases* for allowing us to revise our work. We sincerely hope that our revised manuscript is now suitable for publication.