

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 85034

Title: Gastric neuroendocrine tumors in a BRCA2 germline mutation carrier: A case report

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05342613

Position: Editorial Board

Academic degree: FACS

Professional title: Professor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: China

Manuscript submission date: 2023-04-08

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-04-25 09:28

Reviewer performed review: 2023-04-25 09:32

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

It is interesting that it is the first case detected in a patient with a genetically inherited breast tumor. The clinical picture developed in line with expectations. Histopathological examination was successful. I believe that it will contribute to the literature and readers.

Reply to reviewer:

Thank you for carefully reading my manuscript and providing valuable comments.

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 85034

Title: Gastric neuroendocrine tumour in a BRC Y germline mutation carrier: A case report and review of the literature

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02978155

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Assistant Professor, Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2023-04-08

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-05-20 20:23

Reviewer performed review: 2023-05-25 08:16

Review time: 4 Days and 11 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This paper deals with an interesting topic regarding gastric neuroendocrine neoplasms. However, some limitations should be highlighted 1. The study presents a single case report, which limits the generalizability of the findings. Therefore the conclusion should be more cautious, as case reports provide valuable clinical insights but are inherently limited in their ability to establish broader conclusions or make definitive recommendations. 2. Molecular analysis and significance: While the identification of a pathogenic germline mutation in the BRCA2 gene is noteworthy, the study does not delve into the functional implications of this mutation on the development or progression of gastric NETs. Further investigations are needed to elucidate the precise role of BRCA2 mutations in the pathogenesis of gastric NETs. This should be added to discussion. 3. Treatment implications: The study suggests that PARP inhibitors may be used for type 1 ECL-cell NETs with recurrence, metastasis, or other gastric cancers. However, this recommendation is based on a single case report and lacks clinical trial data or evidence supporting the efficacy of PARP inhibitors specifically in this context. Further research is necessary to validate the therapeutic potential of PARP inhibitors for

this specific subtype of gastric NETs. 4. Instead, as a critique, the authors should have also discussed the potential treatment with somatostatin analogs as an alternative to surgery, as previously described in other studies for the management of unresectable multiple gNENs (PMID 26078554). Indeed, the authors should have addressed the potential use of somatostatin analogs as a therapeutic option for managing multiple gNENs that are not amenable to endoscopic treatment, especially if they are well-differentiated and type 1, as in the case reported. Previous studies have shown good results with somatostatin analogs in controlling tumor growth and symptoms associated with gNENs (PMID: 32213066, PMID: 26321479). Including a discussion on this treatment, modality would have provided a more comprehensive evaluation of therapeutic options for the reported case. 5. Additionally, the histological description of the tumor should be more comprehensive in the "Final diagnosis" section, particularly defining the tumor as well/moderately/poorly differentiated with a mitotic count of 0? and Ki-67 index of 1?. These parameters are crucial in determining the grade and aggressiveness of the tumor and should be explicitly mentioned in the text to provide a more comprehensive understanding of the tumor's histological features. Including these additional discussions and providing a complete histological description would enhance the study's overall scientific rigor and clarity. Finally, the language should be revised. In conclusion, while this study presents an interesting case of a gastric neuroendocrine tumor with a BRCA2 gene germline mutation, several limitations and areas for further investigation should be considered. Future studies with larger sample sizes, comparative analyses, and well-designed methodologies are necessary to validate and expand upon these initial findings and explore the clinical implications in a broader context.

Reply to reviewer:

Thank you for your valuable comments. Based on your comments, the manuscript has been revised again.

1. In the abstract section of the Conclusion, the “For type 1 ECL-cell NETs with recurrence or metastasis or other gastric cancers, PARP inhibitors may be used” has been deleted.
2. At present, the author does not have enough research depth on this case, but the research results of others will be added to the manuscript in the “Discussion” section.
3. Thank you for your kind feedback. I have made corresponding modifications in the manuscript.
4. Thank you for your feedback and the literatures you provided. I have included content on somatostatin analogs therapy for multiple or recurrent gastric NETs in the “Discussion” section, and have cited the literatures you provided. Given the positive upper resection margin in this patient, I will provide a recommendation for somatostatin analogs therapy to the oncologist.
5. I have added the tumor mitotic count in the manuscript. According to the WHO grading classification for digestive system neuroendocrine tumors, the diagnosis is gastric NET, G1. At first, the histological description of the tumor has been in the "Final Diagnosis" section, but the structure of the manuscript is not well connected. Finally, the pathological biopsy were preserved in the "Final Diagnosis" section.
6. The language of the manuscript has been edited by experts again.
7. Finally, thank you for providing valuable insights for my future research on gastric NETs. In our daily work, gastric NETs are frequently encountered, but due to economic constraints and other limitations, it is currently not feasible to perform next-generation sequencing on all all gastric NETs. We will accumulate cases for further study.