

Dear Editor,

We are very glad to receive your reply. We attach great importance to the above questions you raised, and actively deal with the revision and supplementary materials, hoping to meet your requirements. The title of my article: **Tumor recurrence after pathologic complete response in locally advanced gastric cancer after neoadjuvant therapy: case report and literature review.**

Reviewer #1:

Specific Comments to Authors: The authors are presenting a case of Tumor recurrence after pathological complete response in locally advanced gastric cancer after neoadjuvant therapy. Gastric cancer ranks amongst top most cancer worldwide. Usual treatment for locally advanced GC(Neoadjuvant chemo and surgery)have shown little benefit in terms of long term results. The sandwich therapy results are little better. The authors are touching the subject of Neoadjuvant and the combination of immunotherapy. This is a very exciting and promising field and also the value of ypCR. Unfortunately the presentation is very confusing with grammatic errors and also unnecessary text. I suggest , the authors may present this as a short report or a letter to the editor. But before that, the article needs to be rewritten in concise and meaningful way.

Answer: Dear editor, thank you very much for your valuable advice. After re-organizing and repeatedly revising, we finally cut the content of the article by about 30%, making the article more concise and meaningful. We revised the article into a case report. We have also asked a professional company to polish and modify the grammar, hoping to get your approval.

Reviewer #2:

Specific Comments to Authors: Interesting cases but I doubt you may call them rare cases for reporting. There are also some limitations in your approach. Your TNM staging is controversial since both the patients showed positive results in laparoscopic comprehensive exploration and peritoneal lavage for tumor cells, post neoadjuvant therapy that should have been considered distant metastasis and stage IV disease. Moreover, one of the patients was also positive for signet ring cells indicating very poor prognosis. Although there is controversy in the treatment of patients with advanced gastric cancer as your patients, but cytoreduction therapy and intraperitoneal hyperthermic chemoperfusion have been used with some promising results. But local therapy and operation is not recommended. Putting together, recurrence of the cancer especially in the intraperitoneal organs was not unexpected, but rather very expected event in your patients. Moreover, although PD-1 inhibitors have been recommended in patients with metastatic gastric cancer, you've used PD-1 inhibitor Camrelizumab as a neoadjuvant therapy regimen, which is not recommended. Moreover, testing for Her2-NEU was also recommended for targeted therapy.

Answer: Many thanks to the editor for carefully reading my article and asking valuable questions. First of all, I must admit a mistake here. What I wrote in my article was "Laparoscopic comprehensive exploration and abdominal cavity irrigation of tumor cells are positive", but it was

actually "laparoscopic comprehensive exploration and abdominal cavity irrigation of tumor cells are negative". Due to the writing error, the editor eventually misunderstood my article. The previous questions are all based on this mistake, so I hope you can review my article again and give me valuable comments. Thank you very much.

Reviewer #3:

1. Authors are kindly encouraged to include the following references on the role of PD-1/PD-L1 inhibitors in gastric cancer: a.<https://bmccancer.biomedcentral.com/articles/10.1186/s12885-023-10605-y> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7801892/>
b. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6724489/>

Answer: Thank you very much for the important literature provided by the editor, I have added these three documents to the article (References 6-8).

6.Huo G, Liu W, Chen P. Efficacy of PD-1/PD-L1 inhibitors in gastric or gastro-oesophageal junction cancer based on clinical characteristics: a meta-analysis. *BMC Cancer* 2023;**23**:143. [PMID: [36765356](#) DOI: [10.1186/s12885-023-10605-y](#)]

7.Brar G, Shah MA. The role of pembrolizumab in the treatment of PD-L1 expressing gastric and gastroesophageal junction adenocarcinoma. *Therap Adv Gastroenterol* 2019;**12**: 175628481986976 7.[PMID: [31516556](#) DOI: [10.1177/1756284819869767](#)]

8.Voutsadakis IA. A Systematic Review and Meta-analysis of PD-1 and PD-L1 Inhibitors Monotherapy in Metastatic Gastric and Gastroesophageal Junction Adenocarcinoma. *Euroasian J Hepatogastroenterol* 2021;**10**:56-63. [PMID: [33511066](#) DOI: [10.5005/jp-journals-10018-1321](#)]

2. The combined therapy with checkpoint inhibitors with additional antitumor-drugs such as histone deacetylase inhibitors (PD-1/PD-L1 inhibitors), have repeatedly been proposed in cancers (PMID: 35350569 and PMID: 33564072), including gastric cancer PMID: 35008230. This is an important information that should be included in the manuscript alongside the three aforementioned supporting references.

Answer: Thank you very much for the important literature provided by the editor, I have added these three documents to the article (References 2-4).

2.Li X, Su X, Liu R, Pan Y, Fang J, Cao L, Feng C, Shang Q, Chen Y, Shao C, Shi Y. HDAC inhibition potentiates anti-tumor activity of macrophages and enhances anti-PD-L1-mediated tumor suppression. *Oncogene* 2021;**40**:1836-50. [PMID: [33564072](#) DOI: [10.1038/s41388-020-01636-x](#)] [Citation(s) in RCA: 39]

3.Mazziotta C, Lanzillotti C, Gafà R, Touzé A, Durand MA, Martini F, Rotondo JC. The Role of Histone Post-Translational Modifications in Merkel Cell Carcinoma. *Front Oncol* 2022;**12**:83204 7.[PMID: [35350569](#) DOI: [10.3389/fonc.2022.832047](#)]

4. Borcoman E, Kamal M, Marret G, Dupain C, Castel-Ajgal Z, Le Tourneau C. HDAC Inhibition to Prime Immune Checkpoint Inhibitors. *Cancers (Basel)* 2021;**14**:66. [PMID: [35008230](#) DOI: [10.3390/cancers14010066](#)]

3.The staining in fig 1, panel C should be explained in the caption. Is that a specific gastric cancer

marker? Or a HE magnification?

Answer: It's HE magnification.

4. Figures' captions should be in text format

Answer: Thanks very much for the editor's reminder, we have changed the explanatory text of Figures into text format.

5. A brief introduction of both cases should be provided before detailed cases presentation

Answer: Thank you very much for the editor 's opinion, we have added a brief introduction to the case.

6. “discuss! Should be “discussion”

Answer: Thank you very much, has been corrected to ' Discussion'

7. Please check the abbreviations such as OS and DFS which should be explained the first time being mentioned

Answer: Thank you very much, relevant abbreviations have been checked and explained (OS, DFS, ICIS, MSI-H).

Thank you again for reading our work. We are looking forward to hearing from you.

Sincerely yours,

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