

Dear editor:

Please find enclosed the revised manuscript in the supplementary material.

Title: Long-term survival of Gastric Mixed Neuroendocrine-non-neuroendocrine neoplasms (MiNENs): two case reports

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Thank you respectful reviewers for your kind comments on our case report, which gave us the opportunity to revise our manuscript. We emended the paper according to the reviewers' comments. We hope this revision will fulfill the requirements for publication in your journal. Thank you so much.

Reply to reviewers' comments:

1. To reviewer 1

In the revised manuscript (see the supplementary material), we add the incidence of gastric MiNENs and the reference in introduction, as well as the case reports focusing on MiNENs. Until this manuscript were submitted, we haven't found any systemic review about the treatment of MiNEN. However, there are some studies that mention the suggested regimen to MiNENs, and we add those references in our newest revised manuscript. The median survival of gastric MiNEN is less than 12 months, and we added the data this time. To the best of our knowledge, there are no previous studies about using irinotecan plus cisplatin (IP regimen) and curative-intent surgery to treat patients with gastric MiNENs, so our study could be the first. Both our two patients have survived for more than 3 and 7 years, respectively, and are still alive and in good condition, without any evidence of recurrence or metastases.

2. To reviewer 2

We added the pictures of EGD of the two patients in Case 1 and Case 2, with the explanations of the findings. The pathology pictures of them are also in the manuscript.

3. To reviewer 3

The patient in Case 1 received chemotherapy of irinotecan and cisplatin (IP) regimen at first, followed by gastrectomy and hepatectomy. The patient in Case 2 was treated with surgical resection with IP regimen, and recurred lung metastasis was resected two years after that. There was minor difference in the treatment of the two patients, namely the sequence of surgery and chemotherapy, only because they were in different condition and TNM stage when they were first diagnosed. The main idea of our study is that IP regimen and curative-intent surgery - when feasible - could be considered as the new regimen and the priority in the choice of front-line chemotherapy in treating gastric MiNENs. For the reasons above, we thought these two patients could be included in one case report.

The history of the term, MiNEN, and the characteristics of the disease are discussed in the revised manuscript (see the supplementary material). The novelty of our case report is that, to the best of our knowledge, it could be the first time that IP regimen and curative-intent surgery has been used to treat gastric MiNENs. The mistakes in figure legends have been rectified and the dates of CT scan have been erased. Due to the limitation of the number of pictures/tables in one case report and the result of the genetic analysis did not influence the treatment, we only

mentioned the results in the discussion part, instead of in a separate table.

Thank you for considering our case report.

Sincerely yours,

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