November 28, 2020
Dr. Subrata Ghosh
Dr. Andrzej S Tarnawski
Editors-in-Chief
World Journal of Gastroenterology

Re: Manuscript No. 59668. Case Report
Title: “Spontaneous regression of gastric gastrinoma after resection of metastases to the lesser omentum: a case report”

Dear Editors:

On behalf of all the authors, I would like to thank you and anonymous reviewers for their helpful comments. We agree with the points raised and revised our manuscript accordingly. Please find below our point-by-point responses to reviewer comments. We have also made several very minor changes (such as abbreviations) throughout the manuscript.

1. In this case report, it is difficult to distinguish between the simultaneous multicentric gastrinoma of the gastric antrum and the omentum, or the metastasis of the gastric antrum gastrinoma to the omentum. Although the two NETs showed similar histological features and immunohistochemical phenotypes, the evidence here may still be unconvincing. For example, multiple primary NENs in patients with MEN1 could show same pathological changes and immunophenotype. Perhaps the authors could reveal the relationship between the two gastrinomas through further molecular genetic tests. If the two tumors show different molecular genetic changes, it will be more likely to support the possibility of multicentric occurrence. [DOI: 10.1016/j.jamcollsurg.2013.07.402; DOI: 10.1002/(SICI)1096-9896(200001)190:1<76::AID-PATH499>3.0.CO;2-1]

Response:
We thank the reviewer for this brilliant insight and pertinent references. The reviewer correctly points out the most difficult aspect of this case. We devoted an entire section to discuss the difficulty in determining the relationship between the 2 lesions (from LINE 319) but had not considered molecular genetic testing. While we do not have the resources available to conduct such additional testing, we have added a discussion of multicentric occurrence as well as on possible further testing (LINES 385-391).

2. For the Spontaneous regression of gastric gastrinoma, the figure 5B only showed a small amount of superficial gastric mucosa (even can not see the muscularis mucosa) after the previous biopsy. It is difficult to say whether there is any residual tumor in the deep part of the gastric wall, such as the submucosa layer, because NETs are often manifested as submucosal tumors, and previous biopsy may have removed most of the superficial tumor cells. It is necessary to make it clear whether the gastric tumor regressed completely or partially.

Response:
We agree that figure 5B only included the superficial gastric mucosa and that remaining tumor in the submucosa cannot be completely ruled out. As we cannot be certain whether the regression was complete or partial (almost complete), we added a paragraph in the discussion stating that, while we believe a complete regression was achieved, the regression may have been partial (LINES 433-440).

3. Case presentation - the authors mentioned that gastrin decreased to the normal limits. It is necessary mentioning the normal ranges used for data interpretation.

Response:
We added the reference range for serum gastrin at our institution of 37-172 pg/mL (LINES 234-5).

4. Case presentation - Multidisciplinary expert consultation - According to the 5th Edition of the WHO Classification of Digestive System Tumors “blue book”, Mitotic rate of NETs is counted per 2mm2, not per 10 high power fields. Please modify the counting method in the manuscript.

Response:
The reviewer correctly points out that the mitotic rate of NETs should be counted per 2 mm^2. We have corrected the reference to high power fields in the mitotic count (LINE 220).

5. In the legends of Figure 5, it is necessary to make it clear whether the figure 5C is the result of immunohistochemical staining of CgA or the result of Syn.

Response:
We agree that the legend was confusing. Figure 5C was the result of synaptophysin stain. We have corrected this in the figure legend to Figure 5C.

Thank you for your consideration. We look forward to hearing from you regarding our submission. We would be happy to respond to any further questions and comments that you may have.

Sincerely,

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