Dear Editor:

Thank you for asking us to revise our manuscript entitled "Heterotopic pancreas adenocarcinoma in the stomach: A case report and literature review" (ID: 53313). We have finished the revisions following your and the reviewers' suggestions and comments.

Point to point responses to the reviewer's comments:

Reviewer #1(Number ID: 03009363):

Comment : Authors use "mo" instead of month. It sounds a bit slang, I do not advise it in a medical paper.

Response: This has been corrected.

Reviewer #2(Number ID: 03727239):

1. Comment 1: I think the main message of this case is the awareness for malignant transformation of heterotopic pancreas. Therefore, the clinical features of malignant heterotopic pancreas that is different from benign heterotopic pancreas is important. Patient's symptoms are important signs of malignancy as authors described, I think it is also important to diagnose small malignant lesion with no symptoms as reviewed cases. Did the patient in this case or reviewed cases undertake endoscopic ultrasound (EUS) or PET study? And could EUS or PET findings distinguish the malignant and benign lesion?

Response: The above comments and questions are very helpful for improving our paper. It is really true as suggested by the reviewer that it is important to diagnose small malignant lesion with no symptoms. Endoscopic ultrasound was performed in our patient at a local hospital (described on page 3 line 30-32) and 4 patients in the reviewed cases with documented results. In the case reported by Ura et al EUS showed swelling of a perigastric lymph node and changes in mass shape and size, which strongly indicated a malignant lesion.EUS in other cases including ours showed non-specific features such as heterogenous hypoechoic lesion or thickness of the gastric wall. So single EUS detecting for the lesion itself can hardly predict the histologic diagnosis, but

dynamic monitoring and detecting for perigastric lymph nodes by EUS could help distinguishing malignant and benign lesions. PET findings were reported in only one case. In this case, PET scan showed hot spots in gastric wall which indicated malignant lesion. As the lesion size was relatively large (7.5x4.4cm), whether PET scan is helpful to diagnose small malignant lesion still need to be further studied.

We have added this part of discussion to our manuscript (third paragraph in discussion section) according to the reviewer's suggestions.

2. Comment 2: Are there any consensus about the interval of endoscopic examination for surveillance of malignant change of heterotopic pancreas?
Response: To our knowledge, there are now no consensus about the interval of endoscopic examination for surveilance of malignant change of heterotopic pancreas. Dynamic monitoring by endoscopy was performed only in the case reported by Ura et al. In this case, a mass of 1.8 cm ×1.3 cm was detected by EUS and it showed no change 1 year later. However, 2 years after the second examination the mass was found to have increased to 3.3 cm × 3.0 cm and ultimately diagnosed as an invasive adenocarcinoma extending to the peritoneal surface with lymph node metastases. This case suggests that the interval of endoscopic examination for surveilance of malignant change of heterotopic pancreas should be less than 2 years.
We have added a related discussion in our manuscript (third paragraph in discussion section) according to this reviewer's comment.

3. Comment 3:I think Figure 3 is not essential to the present case.
Response: We consider that this comment is correct and have deleted Figure 3 in the previous version of the manuscript.

4. Comment 4: I think the result of immunohistochemical staining is important information in this case, so the figure of immunohistochemical

staining is recommended to add.

Response: This is an excellent suggestion. We have added a figure (Figure 3 in this version of the manuscript) of immunohistochemical staining according to this suggestion.

Reviewer #3(Number ID: 02445734):

Comment: The title of the manuscript and the title of table one is totally misleading. Instead of calling the condition "gastric heterotopic pancreas" which is wrong, it needs to be called "pancreatic heterotopia in the stomach".

Response: We are very sorry for our incorrect writing. We have re-written this part and other parts in the manuscript involving the phrase according to the reviewer's comment.

Other changes:

1. Line 36, Page 4: the statement of "K" is corrected as "cytokeratin".
2. Line 2, Page 6:"However, distinction between benign and malignant lesion is critical for patient management" is added as we think it could help better understanding the thesis of the paragraph.
3. Line 7, Page 6:"In another patient, a mass of 1.8 cm ×1.3 cm was detected by endoscopic sonography and at 3 years later the mass was found to have increased to 3.3 cm × 3.0 cm and ultimately diagnosed as invasive adenocarcinoma extending to the peritoneal surface, with lymph node metastases[17]" is deleted, because it feels redundant.
4.Line 10, Page 6: "Actually, 37.5%of thesecases had a tumorno more than 2 cm." is added to provide an argument for our point.
5. Line 14, Page 6: the statement of "and" is corrected as "or".
6.We have added spaces that were missed in our former manuscript. These changes are marked in red in the revised manuscript.

We hope that the revisions and corrections are valuable and meet your

requirements.

Once again, thank you very much for handling our manuscript.

Xin-Ying Wang

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