August 18, 2017

Damian Garcia-Olm, Stephen C Strom and Andrzej S Tarnawski
Editors-in-Chief
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Dear Editors:

We wish to re-submit the manuscript titled "**Gastric adenocarcinoma of fundic gland type spreading to heterotopic gastric glands**". The manuscript number is 34892.

Thank you very much for considering our manuscript for publication. I am very pleased to see the favorable comments from the reviewers. We have revised our manuscript according to the reviewer comments and feel it is ready for publication in your journal. The responses to all comments have been prepared and given below.

Thank you for your consideration. I look forward to hearing from you.

Sincerely,

Shigeo Manabe
Department of Gastroenterology
Kouseikai Takeda Hospital
841-5, Higashi Shiokoji-cho, Shiokoji-dori
Nishinotoin-higashiiru, Shimogyo-ku, Kyoto 600-8558, Japan
Tel. no.: +81-75-3611351
Fax no.: +81-75-3617602
Email: s-manabe@takedahp.or.jp

Reviewer #03000523

Dear Editor, this is well done case report with literature review. Authors described the case extensively and compare it against the literature. Also they provided excellent documentation and provided all necessary explanations.

Response: Thank you very much for the kind comments. We are very grateful for your appreciation of our manuscript.

Reviewer #02537353

The authors, present a case of gastric adenocarcinoma of fundic gland type (GA-FG) spreading to heterotopic gastric glands (HGG). The topic is adequate for the journal but the scientific impact is low. I suggest a minor language polishing.

Response: Thank you for your suggestion. We have had native English speakers proofread and edit our manuscript and hope it now meets your standards.

Reviewer #02353723

Authors discussed about the relationship between this rare cancer and heterotopic gastric glands, which are considered as a precancerous lesion. However, due to the rarity of this cancer, this association could be a simple coincidence (a role of heterotopic gastric glands has been described only in classic adenocarcinoma). Therefore, more caution is necessary in the discussion.

Response: Thank you for your constructive comments and we completely agree with you. We have described the relationship between gastric adenocarcinoma of fundic gland type (GA-FG) and heterotopic gastric glands (HGG) in our case on page 11, line 23-to page 12, line 4 of the revised version. In addition, we have concluded that GA-FG and HGG in our case were coincidentally present in the vicinity.

Authors did not report any data about proton pump inhibitors (PPI) previous assumption in this patient. This is a key point, due to the causative effect of PPI on fundic gland hypertrophy.

Response: Thank you for your important comments. PPIs were not administered to this patient after *H. pylori* eradication therapy, which was performed 4 years ago. Therefore, it was assumed that fundic gland hypertrophy did not occur in this patient. Moreover, we have now included the additional text about this information on page 7, lines 1- 2 of the revised version.

Recently, Gastric adenocarcinoma and proximal polyposis of the stomach (GAPPS) has been discovered as an inherited syndrome characterized by dysplastic fundic gland polyps. Moreover, familial adenomatous polyposis frequently shows multiple fundic gland gastric polyps. Since both conditions are characterized by APC mutations (see Li L et al, Am J Hum Gen 2016; Mankaney G et al, Fam Cancer 2017), it would have been interesting to evaluate APC mutational status in this patient. Indeed, spontaneous malignant transformation of fundic gland polyps is quite rare.

Response: Thank you very much for your helpful comments. When we performed esophagogastroduodenoscopy for this patient, we did not detect multiple fundic gland polyps of the stomach that would indicate GAPPS. Moreover, when we performed a colonoscopy, there were no colonic adenomas indicating familial adenomatous polyposis. Therefore, although the patient's APC mutational status is unknown at present, this case is not considered to be clinically related to GAPPS or familial adenomatous polyposis.