

Dear Editor,

Thank you for allowing us to submit a revised version of this manuscript. We found the comments from all six reviewers extremely valuable. The comments and suggestions allowed us to improve the manuscript in addition to correcting the errors and mistakes that the reviewers correctly made us aware of. Below, we reply to all comments point-to-point. In the revised manuscript, major revisions are highlighted with [blue](#). The manuscript underwent professional language and style editing, and a language editing certificate is attached with the submission.

All authors approved the revised version of the manuscript. We hope that it may be found suitable for publication in its present form.

On behalf of all authors,

Yours sincerely

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## Point-to-point responses to reviewer comments

### Reviewer #1 (00068458):

Gastric adenocarcinoma of fundic gland is a recently recognized, rare pathologic subtype of gastric adenocarcinoma. The authors submitted well written case report.

R: Thank you for approving our job.

### Reviewer #2 (01209397):

This article is an interesting case report that draws attention to a rare case. However, there is no differential diagnosis. In particular, such low-grade malignancies are confused with regenerative / reactive states. Differential diagnosis is also important with other conditions such as neuroendocrine tumors and fundic gland polyps. the differential diagnosis should be included in the article.

R: The suggested changes were implemented. The sentence was included in the article, showed blue in Line 6-7/Page 9.

### Reviewer #3 (02534438):

Dear Sir, I read with care the manuscript titled "Gastric adenocarcinoma of fundic gland type after *Helicobacter pylori* eradication: A case report". Unfortunately, I can find no new information/originality in this manuscript. I would suggest authors to either re-write it as a review or try to find some original elements.

R: Thanks for your advice. This case report discusses the probability-of-occurrence of GA-FG after *H. pylori* eradication therapy without long-term usage of PPIs. This new information was stated in CORE TIP and CONCLUSION.

**Reviewer #4 (02497698):**

The article entitled "Gastric adenocarcinoma of fundic gland type after *Helicobacter pylori* eradication: A case report" is an interesting, well written article reporting a case of gastric cancer that belong to a recently described histological subtype. There are many cases reported from eastern countries but this histological subtype is rarely mentioned in western countries. Because of this, the detailed descriptions of the diagnostic procedure and the follow up, the possible relationship with *Helicobacter pylori* and the histological analysis are important. The introduction and the discussion are concise and precise, and the results are well described, making all the article easy for reading and understanding. I found interesting the clinical data and the histological analysis, but a description of the antibodies used and the immunohistochemical procedure is necessary.

R: Thank you for approving our job.

**Reviewer #5 (01430832):**

1 The number of cases reported in the literature should be mentioned (see Benedict et al.)

R 1: We have rewritten the sentence in Line 17/Page 8.

2 In the introduction the sentence "The tumor had invaded the submucosal layer" is out of context.

R 2: Thanks for your advice. We have rewritten the sentence in Line 18-20/Page 5.

3 Why an annual gastroscopy was done after Hp eradication?

R 3: The patient was followed up with annual gastroscopy because of CAG. The sentences were changed in the revised manuscript (Line 2-8/Page 6).

4 In the reviewed by Benedict, 40% of the cases was Hp positive. So the

presence or not of Hp does not seem to be relevant.

R 4: Yes, “Of the 111 cases of GA-FG published, H pylori data were available in only 43 (39%) cases, of which 17 (40%) were positive for infection.” Although GA-FG is generally thought related to non-atrophic mucosa and H. pylori negative, it has been reported to occur with a history of H. pylori eradication[Chiba T, Kato K, Masuda T, et al. Clinicopathological features of gastric adenocarcinoma of the fundic gland (chief cell predominant type) by retrospective and prospective analyses of endoscopic findings. Dig Endoscopy 28: 722-730, 2010.]. Our patient had a history of H. pylori eradication therapy twice, supported this viewpoint.

5 What about the result of the endoscopies? Were FGP found in other sections of the stomach to support an association between them and GA-FG?

R 5: Endoscopic findings were showed in the section of “Imaging examinations”. No FGP was found in other sections of the stomach. It's a solitary tumor.

6 The authors should emphasize the differences between their case and the cases previously reported mainly the location (only 1% are found in the lower third) and the lack of the sequence PPI to FGP to GA-FG (the patient did not take PPI ).

R 6: Thanks for your suggestion. In our patient, the GA-FG was localized in the lower part of the gastric body, i. e., the middle third of the stomach (18% reported by Benedict et al). Our patient had no history of long-term medication of any PPIs and had no FGP in other sections of her stomach, it is unclear whether there was a relationship with PPIs use. We have rewritten these sentences in the revised manuscript.

**Reviewer #6 (00503623):**

The manuscript reports the case of gastric adenocarcinoma of fundic gland

type (GA-FG) found in a 77 years old woman who has undergone previously two eradication therapies for Hp without the use of proton pump inhibitors. The case is quite interesting, however there is no information provided as to the current actual Hp status of the patient nor there are any data on the type of therapy used for Hp eradication.

R: The suggested changes were implemented. The patient had received recommended dose of *H. pylori* eradication therapy twice, once 7 days for omeprazole + amoxicillin + clarithromycin and once 14 days for pantoprazole + bismuthate + tetracycline + metronidazole (Line 4-7/Page 6). Atrophy of the gastric mucosa was classified as C-2, yet the local background mucosa of the lesion showed no apparent atrophy, after eradication of *H. pylori* (Line 28-30/Page 6). Thank you.