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Lian-Sheng Ma,
Editor-in-Chief
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Manuscript # 21635: “**The diagnosis of follicular lymphoma of the gastrointestinal tract: A better initial diagnostic workup**” by Iwamuro et al. (Number ID: 00070922).

Dear Dr. Ma:

We hereby resubmit our above-named manuscript for reconsideration for publication in *World Journal of Gastroenterology*. We have carefully considered all of the enclosed comments and addressed them as thoroughly as possible. Point-by-point responses to the comments of the reviewers are given below. We hope you will find our revised manuscript now acceptable for publication in *World Journal of Gastroenterology*. Thank you for your consideration.

Sincerely yours,

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Manuscript # 21635: “The diagnosis of follicular lymphoma of the gastrointestinal tract”

Point-by-Point Responses to the Reviewers' Comments

Reviewer #1

GENERAL COMMENTS. The aim of this interesting review is to give guidelines for optimal diagnostic strategy of for patient with the gastrointestinal primary or secondary localizations of follicular lymphoma. The authors provide adequate analysis and comprehensive discussion which could be more a proposition of management than real guidelines, on the basis of the current literature and their own experience, the authors should avoid the term “guidelines” which is reserved for a specific and well defined form of recommendations. Furthermore, the major part of the description and references in this review deals with primary gastro-intestinal follicular lymphoma. So to our opinion this review should exclude secondary gastrointestinal involvement of nodal (not systemic as cited) follicular lymphoma. Indeed, the extra nodal primary gastro-intestinal type of follicular lymphoma is rare and of interest comparing to the nodal follicular counterpart which often involves gastrointestinal tract at advanced stage IV.

In this review the most interesting information and useful data for clinician and mainly gastroenterologist reported are the descriptions of the different clinical, endoscopic features and magnifying endoscopy observations and mainly concerned primary gastro-intestinal follicular lymphoma.

In addition this review is much too long and should be restricted to the specificity of gastrointestinal primary localization of follicular lymphomas. Staging, histology classification and score descriptions for these lymphomas are already well known because same as in frequent nodal lymphomas and seem not so interesting for this review and they should be shortened. Same for remark concerning the interest of CT scan and serum soluble IL-2R levels and FLIPI score.

Thank you very much for taking the time to review our manuscript.

In our manuscript, I have carefully avoided using the term “guidelines” and have instead used the phrases “strategies” or “pearls and pitfalls.” In addition, I have rewritten the first sentence of the conclusion to clarify the meaning.

In order to focus on primary gastrointestinal follicular lymphoma and to cut down the length of our review paper, I have deleted descriptions relating to nodal follicular lymphomas; I have deleted five sentences in the “Clinical and laboratory assessment” section, seven sentences in the “Histological assessment of biopsied specimens” section, 20 sentences in the “Staging” section, two sentences in the “Soluble interleukin-2 receptor” section, three sentences in the “Pathogenesis” section, and two sentences in the “Risk assessment according to the FLIPI and FLIPI2 scores” section. I have also removed 14 references.

After considering that although gastroenterologists are responsible for the initial diagnostic workup of this disease in a considerable proportion of cases, many gastroenterologists are unfamiliar with lymphoma staging, histology classification, and FLIPI scores. Therefore, I have retained some information about these topics in the review.

Finally, discussion concerning H. pylori which is to our opinion irrelevant. Indeed the role of H. pylori in the pathogenesis of follicular lymphoma has never been proved. However spontaneous regression of these lymphomas, as mentioned by the authors, has already been described and is interesting to discuss.

We totally agree with your comments. Although regression of intestinal follicular lymphoma lesions has been described in several case reports, we are skeptical about the role of *H. pylori* in the pathogenesis of this disease. To clarify this issue, we changed the subheading to “Pathogenesis” and added one paragraph.

(1) the overall structure of the manuscript complete;(2) taking general comments into account, the manuscript would be interesting enough to warrant the readers' attention;(3) Endoscopic features, magnifying endoscopy observations reported from literature and own author experience are of interest with adequate details to guide the gastroenterologist for primary gastro-intestinal follicular lymphoma diagnosis;(4) The author use appropriate citations to support the information presented throughout the main body of the manuscript. (5) The authors provide adequate analysis and comprehensive discussion on the basis of the current literature and their own experience; (6) The conclusion point out contribution of the review for rather say “a better diagnosis” (instead of “guidelines”) for managing gastro-intestinal follicular

lymphoma and the importance of endoscopic examinations.(7) The manuscript cite all important, relevant and timely references but they should be restricted to gastro-intestinal follicular lymphomas for this review (some references to be deleted) ; (11) the manuscript gives interesting and exhaustive descriptions of gastrointestinal follicular lymphoma helping for diagnosis of such tumours.(12) The title of the manuscript contain key words and should perhaps include the term of primary gastro-intestinal follicular lymphoma (13) The topic of the manuscript fall within the scope of World Journal of Gastroenterology.

Thank you very much for your comments. I have reduced the length of the article and removed a number of references.

SPECIFIC COMMENTS. (1) Figures 1 and 2 (magnification to be completed) are well presented and of interest.(2)Table 1 and 2 if maintained should replace paragraph 1 and 2 and perhaps even table 2 deleted. (3) in comments radiotherapy is often cited as localized treatment : this is not adapted to intestinal localization even at stage I. (4) first sentence of conclusion should be rephrased.

Tables 2 and 3 have been removed.

In accordance with your comments, I have removed the words “local” and “as a local treatment.” As explained above in the Responses to Reviewer #1, I have rewritten the first sentence of conclusion.

CONCLUSION: this manuscript is concise, clear and comprehensive. The experience and lessons presented in it aim at improving the readers' practice on this rare entity, especially concerning clinical and endoscopic diagnosis of gastrointestinal primary follicular lymphoma. However, for well-known data (such as histology classification, staging, CT-scan valuations and scores) concerning also the nodal counterpart of these follicular lymphomas, the text should be shortened and some references deleted. After fulfilling these conditions, the content of the manuscript will be acceptable for publication in the World Journal of Gastroenterology

We hope you will find our revised manuscript acceptable for publication. Thank you for

your consideration.

Reviewer #2

GENERAL COMMENTS: *This paper focuses on the optimal diagnostic strategy for patients with primary gastrointestinal follicular lymphoma or secondary gastrointestinal involvement of systemic follicular lymphoma. Authors collected case reports, case series, and retrospective studies in relation to follicular lymphoma of the gastrointestinal tract. The endoscopic and histological features, the roles of CT and PET scanning, the clinical utility of the soluble interleukin-2 receptor, and the possible etiological role of Helicobacter pylori were in detail reviewed. Authors also mentioned their own experiences about the diagnosis of follicular lymphoma in the gastrointestinal tract. Therefore this review is helpful for a better understanding of the diagnosis and initial workup about the follicular lymphoma in the gastrointestinal tract. The manuscript is good for the readership of WJG, especially for the gastroenterologist and patients with lymphoma, even relevant for the normal population.*

Thank you very much for your comments.

SPECIFIC COMMENTS:

- (1) The overall structure of the manuscript is nearly complete. Perhaps the running title should be provided in the title page.*
- (2) The Introduction section of the manuscript clearly presented the pathological features detection methods of the follicular lymphoma and the purpose of this review.*
- (3) The authors adequately understand and cite all of the important references to support the overall explanation of the review.*
- (4) The authors provided comprehensive discussion on the basis of the cited literatures.*
- (5) The conclusion is clear and well.*
- (6) The manuscript cited all important and relevant references.*
- (7) The manuscript is based upon a summarization of the literatures and authors own publications in the field of follicular lymphoma in the gastrointestinal tract.*
- (8) On the basis of knowledge about the diagnosis of follicular lymphoma in the gastrointestinal tract, authors also provided some useful suggestions for the diagnosis according to their understanding and own experiences in relation to follicular lymphoma*

in the gastrointestinal tract.

(9) The title of the manuscript contains key words, and the title is interesting enough to attract readers' attention.

(10) The topic of the manuscript is suitable for World Journal of Gastroenterology.

(11) The language of the manuscript is ok and only need to minor improvement.

Thank you very much for your comments. I have added a running title to the title page.

MINOR COMMENTS:

(1) Please inserting page number.

I have inserted page numbers into the header of the document.

(2) Please adding subtitle.

I have added a subtitle and modified the title of our manuscript as follows: The diagnosis of follicular lymphoma of the gastrointestinal tract: a better initial diagnostic workup.

(3) The descriptions of paragraph 1 and 2 at page 12 are completely repeated with Table 2 and Table 3. Therefore it is suggested to delete either paragraph 1 and 2 or Table 2 and 3.

In accordance with your comments, I have deleted Tables 2 and 3.

(4) Please clearly indicate the magnification of Fig. 2A, B, C, D, E, F.

I have corrected the description. The characters indicating the magnification were corrupted and have been replaced.

CONCLUSIONS: *The manuscript is concise, clear, comprehensive, and convincing. The content of this review has value for publication. However the authors should make*

minor revision before accepting for publication in WJG.

We highly appreciate your comments.