September 15, 2019

Dear Members

Editorial Office

World Journal of Gastrointestinal Surgery

Reference: Revised Manuscript ID 51053

Title: "Early pancreatic cancer in IgG4-related pancreatic mass: case report and review of the literature"

Dear Sir:

We thank the referees for their fair, thorough and thoughtful review. Please see below our response to their comments. All the concerns raised by the reviewers have been addressed, and we hope that you will find the revised manuscript suitable for publication.

As suggested in the "Edited Manuscript by Editor" the following changes were also acknowledged:

- Review and update of all references.
- Correction of the figure legends.

On behalf of the co-authors, I would like to thank the reviewers for their helpful and cogent comments.

All the authors have seen this version of the manuscript and agree with the modifications that have been performed.

Reviewers' comments:

Reviewer #1:

Comment 1: The authors present a case where possibily a pancreatic cancer with a IgG4 disease coesists. A Major issue of this paper is the Histopathologic diagnosis of the IgG4 Disease. IgG4 Staining can Show a dense plasmacell Infiltrate in many cases, also without IgG4 Disease. The histopathological diagnosis should be done using the Honululu concensus criteria (Chiari et al., Pancreas). If such criteria are positive, a diagnosis can be made (Plasmacellinfiltrate, dense IgG4 Staining, venulitis, Arteritis). The pathologist should revise the slides and apply such criteria. Ductal Adenocarcinomas are sometimes seen in concomitance with IgG4 Disease, and PANIN lesions are also often seen in specimens with autoimmune pancreatitis. Acinar

adenocarcinoma is rare with a IgG4 disease. Response to steroid is typical of IgG4 disease, so diagnosis may be possible. However, histopathological criteria for diagnosis should be applied.

- Response: We thank the reviewer for the valuable and constructive comment. We agree to fit the histopathological findings within Honolulu Consensus criteria.
  Consequently, we have modified the paragraph of the "Outcome and Follow-up" section -where the histopathological report is described- as follows:
  - *"On histopathological revision of the resected specimen, and surrounding the neoplastic lesion, pathologic characteristics of IgG4-related disease (LPSP) could be recognized. There was an intense lymphoplasmacytic infiltrate predominantly on a periductal fashion, a trabecular fibrotic pattern and focal vascular structures with obliterative phlebitis. After immunohistochemical evaluation, most of the plasma cells were IgG positive with more than 50 IgG4 positive plasma cells/high power field and an IgG4/IgG ratio greater than 40%. (Figure 3. A,B,C,D,E).*
    Since the lesion met most of the "Honolulu Consensus Criteria" a diagnosis of AC-PC in a context of a probable IgG4-related disease was made.
    The clinical context in addition to the histopathology and immunohistochemistry allowed to infer a sistemic IgG4-related disease."

We also updated the references by adding the suggested paper (*5. Chari ST, Kloeppel G, Zhang L, Notohara K, Lerch MM, Shimosegawa T. Histopathologic and clinical subtypes of autoimmune pancreatitis: the Honolulu consensus document. Pancreatology. 2010;10(6):664-72. PMID: 21242705; DOI: 10.1159/000318809).*

Reviewer #2: No specifics comments to the authors.

Please do not hesitate to contact me if there is any further revision of our manuscript needed. Looking forward to a favorable response, I thank you in advance.

Sincerely,

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