ANSWERING REVIEWERS

April 1st, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Type1AIPRevision.doc).

Title: Clinical and Pathological Differences between Serum IgG4-positive and IgG4-negative Type 1 Autoimmune Pancreatitis

Author: Woo Hyun Paik, Ji Kon Ryu, Jin Myung Park, Byeong Jun Song, Joo Kyung Park, Yong-Tae Kim and Kyoungbun Lee

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The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer
Reviewer 1
Comments: 1. The authors used the updated criteria to classify the type 1 and 2 AIH and stained/measured IgG4. It is better if the authors to have the ratio of IgG4/total IgG. It may be difficult to have the total IgG measured in blood, since this is a retrospective study. However, you may still have the paraffin block to do the total IgG staining.

Paraffin blocks are available in only some cases because this is a retrospective study from 2005 to 2011. So, it is impossible to do total IgG staining in all patients. In addition, total IgG staining is not included in ICDC and total IgG staining is not necessary in this study.

2. Both the serum-positive and negative AIPs received steroid treatment, did they have similar response? As to the relapse, it is better to mention how long it relapsed after the steroid treatment.

We corrected and added some sentences in result.

All patients except surgical resection received steroid treatment and the response rate was 100% in both SIP and SIN groups. The relapse rate was not different between two groups (36% vs. 25% in SIP and SIN group, P=0.80). The mean interval from steroid treatment and relapse was not different

between two groups (14 vs. 11 months in SIP and SIN groups, *P*=0.82).

3. The authors excluded 8 cases (no histology and normal serum IgG4). I wonder how these 8 patients were treated? If treated with steroids, any response? Any follow-up?

We added some sentences in discussion.

The 8 patients received steroid treatment and steroid responsiveness was 100%. One patient experienced relapse.

4. The extrapancreatic involvement was diagnosed with imaging. Any of them with pathology (resection, biopsy) evidence?

We added some sentences in results.

Only one patient with sclerosing cholangitis was pathologically confirmed as an other organ involvement and other patients were diagnosed with only image and steroid responsiveness.

5. The surgical resection rate was higher in SIN group than that in SIP group. Any explanation on that? Some cases were diagnosed in early years, any difference between early and late years?

We added some sentences in discussion.

The surgical resection rate was higher in SIN than SIP group. The one reason could be a difficult diagnosis of AIP. If the lesion is in the body/tail and serum IgG4 is normal, the clinicians can`t suspect the possibility of AIP and don`t hesitate surgical resection. Another reason might be selection bias of this study because we excluded 8 patients with normal serum IgG4 and no histology. The 8 patients received steroid treatment and steroid responsiveness was 100%. One patient experienced relapse.

6. The authors mentioned their surgeons had a few concepts about AIP in early period. I don’t understand this sentence well. Please explain.

We corrected and added some sentences in result

However, surgical resection was done in two cases because serum IgG4 was normal and possibility of malignancy could not be excluded in early period (2005).

7. In the discussion, the authors mentioned there were only 2 studies on IgG4 negative AIP. Please do pubmed search again and you will find more than 2 studies.

We corrected it.

Unfortunately, there were a few studies about the normal serum IgG4 AIP till now.

8. For fig. 2, it is better to show 2 separate charts to demonstrate SIN and SIP patients.

We corrected it.

9. For fig 3. It is better to draw arrows on both panels to indicate the changes. Not all readers can read MRI.

We corrected it.

10. For Fig. 4, only high power picture with IgG4 staining was shown. I would like to see several typical pictures of type 1 AIH with IgG4 IHC staining.

We added the figure.

11. I would suggest a degree of technical editing to improve some points of English grammar.

We corrected it.

Reviewer 2

1. The ration of IgG4/IgG-positive plasma cells in resected or biopsied specimen is required. This ration is included in the diagnostic criteria of IgG4-related diseases as well as the count of IgG4-positive plasma cells.

Paraffin blocks are available in only some cases because this is a retrospective study from 2005 to 2011. So, it is impossible to do total IgG staining in all patients. In addition, total IgG staining is not included in ICDC and total IgG staining is not necessary in this study.

2. The histopathological picture of serum IgG4-positive AIP.

We added the figure.

Reviewer 2

1. In the paper, "AIP was diagnosed by ICDC" is described. Were they diagnosed as definite or probable? How were SIN cases diagnosed by ICDC? Diagnosis of each case by ICDC should be presented in detail.

We corrected and added some sentences in manuscript.

We enrolled the patients with definite AIP.

Six patients who received surgical resection could be confirmed as type I AIP with LPSP (level 1 criterion) and level 1/2 parenchymal imaging. One patient (case 3) had level 1 parenchymal imaging and level 2 histology. The other patient (case 4) could be diagnosed as type 1 AIP with level 1 ductal imaging, level 2 histology and response to steroid.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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