Dr. Yuan Qi,
Science editor, Editorial office, Baishideng Publishing Group Inc

Jul. 7th, 2016

Dear Dr. Yuan Qi

On behalf of all the authors, we thank you for reviewing our manuscript entitled "Pancreatic neuroendocrine tumor and solid-pseudopapillary neoplasm: key immunohistochemical profiles for differential diagnosis". We revised our manuscript according to the reviewers' and editor's comments. So we wish our manuscript will be published in the World Journal of Gastroenterology.

Sincerely,

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Yusuke Ohara, MD, PhD

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Comments to Authors

REVIEWER 1

Large number of patients is needed to assess the feasibility of these markers.

Answer to the comment

Thank you for your comment. Surely small number of patients was enrolled in this study, because SPN is rare tumor among pancreatic neoplasm. So we mentioned that as the limitation of our study.

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The limitation of our study is that the number of cases we evaluated was small because SPN is rare pancreatic tumor.

REVIEWER 2

1. Determination of hormones is helpful for diagnosis of NET. 6 NET were insulinomas, 4 were MEN I. For the other 14 patients the results of preoperative determination of glucagon, somatostasin or gastrin should be added (negative or not done)

Answer to the comment

We added the sentence about blood examination for hormone.

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the other 14 (NET-11 to NET-24) did not have any genetic background, symptoms or blood examination data attributable to hormone hypersecretion.

2. Because of beta catenin gen mutation beta-catenin shifts to the nucleous carrying along E-cadherin. Therefore in SPN there is a loss of membrane staining and nuclear positivity for beta-catenin and E-cadherin . This mechanism should be mentioned for better understanding. In the method and in paper should be mentioned that the results of E-cadherin refer to membran staining and the results of beta-catenin refer to nuclear staining. In Table 3 "?cat (N)" probably is correct and not "?cat (N/C)".

Answer to the comment

We had described about ß-catenin accumulation in the nucleus in Discussion session.

So we added the sentences. Earlier studies showed the ß-catenin staining of SPN as Nuclear/Cytoplasmic staining, so we assessed ß-catenin staining as N/C pattern (Kim et al. Human Pathology, 2008).

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Abnormal accumulation of ß-catenin in the nucleus, caused by prolonged degradation of mutated ß-catenin protein correlated with loss of E-cadherin, was observed in 95% of SPNs

3. The authors should give reasons for selected 9 markers. For diagnosis of SPN CD 56, NSE, Cylclin D1, Synaptophysin and others are recommended too.

Answer to the comment

We chose 9 markers based on earlier reports (see references). Synaptophysin was already examined (see tables). CD56 and NSE had been examined in our preliminary examination; however, these markers were positive in most NET and SPN, therefore we did not select these markers.

4. The chapter Immunohistochemical findings should be shortened. The first and the second paragraph partially contain the same results. A table with positive and negative results for each marker in NET and SPN would give a better overview.

Answer to the comment

In the chapter of Immunohistochemical findings, the first paragraph described the immunohistochemical data and the second paragraph stated the interpretation of the data. Previously we had restructured this chapter as shorter version; however, we supposed the contents of the result, especially about NET-23 and -24 (confusing cases), might be misunderstood by readers.

So we wish this chapter is kept as present style.

5. The limitations of the paper should be added.

As the reviewer said, the limitation of this study was the small numbers of cases was enrolled in this study. So we added the sentences about limitation of our study.

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The limitation of our study is that the number of cases we evaluated was small

because SPN is rare pancreatic tumor.