Reviewer’s report

Title: Chinese siblings with hereditary medullary thyroid carcinoma caused by RET mutation: implications for RET oncogene detection

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Reviewer: Kenji Ashida

Reviewer's report:

General comments to the authors:

Authors described the two cases with familial medullary thyroid carcinoma caused by p.C620Y mutation in RET oncogene. This is a first report of Chinese, although the mutation is a common mutation in the world. Because the patients with this mutation show wide range prognosis as shown in this report, physicians cannot conclude the handling of this case. Further case studies and investigations are required to evaluate significance of occult p.C620Y RET oncogene mutations on the prognosis.

Authors described important practical issues. However, revision of the manuscript is required to clarify there intended meaning and to realize what physicians should remind from this manuscript. In addition, authors clarify and generalize what is the clinical importance in this manuscript that described first case series in China. These revisions can make this article more comprehensive and attractive for the readers in this journal.

Minor comments:

Title and abstract:

"A rare C620Y variant in RET in Chinese family" is not good, because it may contain alternative meaning. First: C620Y mutation is rare in familial MTC. Second: C620Y mutation is rare in China.

In addition, "A rare C620Y variant in RET in Chinese family" means C620Y mutation is rare among the various mutations in RET oncogenes in Chinese. In China, do physicians examine the RET oncogene mutation in dairy clinical work? What is the dominant mutation in the sporadic MTC?

(Endoscopic) ultrasonography could detect MTC, however, could not confirmed.

If authors use MTC for abbreviations, unify throughout the abstract.

Background:
Because authors emphasize the importance of p.C620Y mutations in RET, description about pC620Y mutation helps readers to understand the importance of this report.

In addition, is MTC frequency in China different from other countries?

**Case presentation:**

Patient 1

How about the calcitonin and CEA levels? After the total thyroidectomy with lymph node dissections, these levels decreased to reference levels? In addition, patient is planned for further chemotherapy for residual FMTC?

How about the hyperparathyroidism or pheochromocytoma as MEN type 2?

How about the hypoparathyroidism after the total thyroidectomy? Is the parathyroid gland could be preserved?

Patient 2

"….. vitamin D3 tablets (Ⅱ) at a dose of 50 g … (Line 50, page 3)" &lt;/i&gt; What is "Ⅱ"?  

**Follow-up and outcomes**

Describe the details about missense mutations of p.C620Y. Substitution of base.

Why do the authors evaluate the patients as satisfactory therapeutic results? How about the metastasis? Did authors explore? Detailed description is required, because they discuss the importance of p.C620Y mutation on prognosis of the patients in followed discussion section.

**Discussion and conclusions:**

"Currently, more than 100 RET ….. extracellular cysteine-rich domain [4]. (Lines 67 to 69, page 3)" and "This variant is ….. no more than 1% [5, 6] (Lines 71 to 72, page 4)"

Authors described codon 620 is common mutation; however, p.C620Y mutation is no more than 1%. Other mutations in codon 620 have specific phenotypes? Authors discussed clinical features of p.C620Y and their cases, however comparisons with other common mutations in p.620 may help readers' understandings.

"Our report also …. counseling in MTC. (Lines 90 to 91, page 4)." &lt;/i&gt;&lt;br&gt; Authors do not describe the importance of counseling in manuscript. If the authors conclude that issue, denote that issue in the manuscript.
Tables and Graphics

Figure 1(E): Single parent can produce child?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Unable to assess

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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