Reviewer’s report

Title: Papillary thyroid carcinoma with pleomorphic tumor giant cells in a pregnant woman - a case report

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Reviewer: Naoki Oishi

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This is a case report by Paulsson et al. describing a papillary thyroid carcinoma with pleomorphic tumor giant cells (PTC-GC) in a 28-year-old woman. Since PTC-GC seems to have more favorable outcome than PTC with minor anaplastic carcinoma component [such as PTC with spindle and giant cell carcinoma (PTC-SGC)], they tried to distinguish it conducting genetic testing for BRAF, TP53, and TERT. Overall, this is a well-written paper; however there are some major and minor criticisms.

Major

1) Were the pleomorphic giant cells in the PTC identified on the preoperative cytology? If present, it is interesting and important to recognize the potential diagnostic pitfall to misdiagnose PTC-GC as anaplastic thyroid carcinoma (ATC). Therefore, authors should describe whether there pleomorphic giant cells were positive or negative in cytology.

2) Authors reported that the PTC-GC exhibited necrosis in its conventional PTC area. Is it real necrosis (due to high proliferation) or secondary necrosis after puncture of fine needle aspiration? Please provide a microscopic photograph if necessary.

3) Authors should discuss how these giant cells are developed in the PTC. Follicular adenomas (FAs) may exhibit focal pleomorphism with bizarre nuclei, which are largely considered to be degenerative changes, and such pleomorphic FAs are referred to as "FAs with bizarre nuclei" according to the new WHO classification. It would be better to discuss the similarity and difference between the pleomorphic cells seen in PTC-GC and FA with bizarre nuclei.

4) Authors reported that they diagnosed this case as PTC-GC largely depending on the results of molecular testing: absence of TP53 and TERT promoter mutation, since TP53 and TERT promoter mutations are shown to be associated with anaplastic transformation. However, even before conducting molecular analysis it is highly unlikely that TERT promoter mutation occurs in such a young patient, because TERT promoter mutation has strong association with older patient's age. Actually, there have been only few TERT-mutated
PTCs reported in patients younger than 40 years old. Therefore, it is still obscure whether genetic testing for TERT promoter mutation is useful in such a young patient. The authors must discuss the association between patient's age and TERT promoter mutations before they stress the importance of genetic testing.

Minor

1) Although authors provided Ki67-labeling index (around 30%) in the pleomorphic area, they should also note the mitotic counts there.

2) The word "proliferation counts" is confusing. Please clarify whether it means "high mitotic counts" or "high Ki67-labeling index" in each time.

3) In background, "how different clinical, histological and immunohistochemical analyses was used" should be modified to "how different clinical, histological and immunohistochemical analyses were used".

4) In Case Presentation, the level of thyroglobulin ("0.2") should be noted with appropriate unit.

5) In Figure Legend "e", it should be clearly annotated that it is immunohistochemistry for Ki67.

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

Yes

**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.

No
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

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