

February 15, 2022

To: Editor
World Journal of Clinical Cases

RE: Manuscript NO: 73865

Dear editor:

Thank you for the opportunity to revise our manuscript "Metaplastic Breast Cancer with Chondrosarcomatous Differentiation Combined with Concurrent Bilateral Breast Cancer: A Case Report and Literature Review ". The reviewers' and editors' comments were useful and helped to clarify and improve several aspects of the manuscript.

Please find attached the revised version of the manuscript, with all amendments highlighted in red. Below is a point-by-point response to the issues raised by the reviewers and editors. This revised manuscript has been edited and proofread by *Medjaden* Bioscience Limited. We hope that this version is suitable for publication in the World Journal of Clinical Cases.

We look forward to hearing from you.

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Point-by-point response.

Science editor:

The manuscript elaborated a case of metaplastic breast cancer with chondrosarcomatous differentiation combined with concurrent bilateral breast cancer. It seems the case was in the rare situation and therefore, can be considered for further review in this journal, however, there are several concerns to be clarified prior for the further review. The discussion needs to be improved, and the logic is not very good. Case presentation should be divided into several chapters according to the relevant requirements of this journal.

Response: We have revised the whole manuscript according to the requirements of this journal. More necessary details of the case were supplied. In addition, the discussion section was revised to make it logical.

SPECIFIC COMMENTS TO AUTHORS

The manuscript by Siyuan Yang et al reports the case of a patient affected by metaplastic breast cancer, a rare breast cancer subtype herein presented with a chondrosarcomatous differentiation, combined with concurrent bilateral breast cancer. This case can be considered extremely rare. The patient was treated with neoadjuvant chemotherapy after which both the masses partially responded. The left mass showed a chondrosarcoma component which was not detected using needle biopsy, reason why the patient was treated with neoadjuvant therapy and treated as a non-metaplastic breast cancer. The patient was then subjected to adjuvant therapy with good results. In the discussion the authors treat about the rarity of this case and talk about the heterogeneity-related issues and the concerns associated with the possibility for core needle-biopsy to give non-representative information of the whole tumor, as for this case. Considered the rarity of metaplastic breast cancer, this manuscript has the potential to give a little contribution to the literature about this disease. However, I think that the manuscript needs some work to make it more readable. Ambiguities should be solved.

Major comments:

Lines 147-165: this part of the discussion is very confusing. I think that a re-read should make it more readable. For instance, what do the authors mean for "Waveform proteins"? The research on PubMed for this term did not bring any results, can the authors please clarify?

Response: It should be the word of "vimentin". We have revised the sentence accordingly (page 9, line 177 & line 179).

What do the authors mean with "chemotactic component" and "chemogenic component"? Please clarify.

Response: Sorry for the mistakes. The right term for them should be the “metaplastic component.” We have revised the terms accordingly.

Abstract reports: "Following this, the patient was switched to continuous treatment with endocrine therapy using letrozole + goserelin, and the patient is currently in stable condition. " Whereas discussion reports "The patient is expected to take capecitabine for 6 months, after which, she will be treated with letrozole + goserelin for endocrine therapy. " It is not clear if the patient has already started this therapy or if she is going to. Please clarify.

Response: Sorry for the mistake. We have revised the sentences as the following “The patient has taken capecitabine for 6 months, after which, she was treated with letrozole + goserelin for endocrine therapy.” See page 7, lines 134.

In the abstract: "Postoperative pathology suggested carcinosarcoma with predominantly chondrosarcoma in the left breast (triple-negative cancer component)" and in the manuscript (lines 107-108): "immunohistochemical findings of ER (–), PR (+, 5%), Ki-67 (+, 70%) for invasive ductal carcinoma". Please clarify.

Response: We considered it as a TNBC as the PR expression is too low (5%). However, we agree with the reviewer and delete the phrase “triple-negative cancer component” from the abstract.

In the discussion the authors say that needle biopsy can fail to provide complete information also due to the heterogeneity in cell population. Do they think that, in case of inoperable tumor, there could be other tools for unravel this issue? A sentence concerning this concept could be important.

Response : In our experience, it is possible to obtain more pathological tissue through multiple punctures at different sites for inoperable tumors using the Core needle biopsy. However, multiple punctures can significantly increase cost and patient pain. Furthermore, it may even lead to life-threatening severe events such as major bleeding, so we did not perform multiple punctures in this case (page 8, lines 161-165).

The quality of figures 3,4,5,7 is poor, and a scale is lacking.

Response: We have updated the figures with higher quality and added the scale.

Minor:

Line 103: MRI is reported twice.

Response: Sorry for the typo. It should be MRI showed significant regression of the left breast mass (Figure 6) (page 7, line 122).

Please ensure that full name is reported every time an abbreviation is used and ensure that abbreviations are always used along the next (for example line 163: "metaplastic breast cancer" should be "MPC").

Response: Thank you for pointing this out. We have rechecked the whole context to correct all the mistakes like this.