Peer Review File

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Reviewer A

First of all, thank you for your valuable comments on this paper. In response to your questions, our specific responses and modifications are as follows:
1.The introduction is too long.
Response: As suggested, we have deleted a portion of the introduction to make it more concise. (See page 2 lines 100-108)

2.The chemotherapy protocol is not described in detail.
Response: We appreciate the reviewer's more accurate description. We have supplemented detailed information on chemotherapy drugs. (see page 6， lines145-146, page7 lines 198-199)

3.The contributions of other authors apart from YZ and DL are not mentioned.
Response: As suggested, we have supplemented the contributions of several other authors. (see page 1, line 26-27)

Reviewer B

The paper is well written and valuable, but it is somewhat difficult to follow and it seems that some of the important information and some of the data/information to support the authors' conclusions are missing or not well described.
Response: Firstly, thank you for your support and recognition of this paper and your valuable comments on this paper. In response to your question, our specific responses and modifications are as follows:

1. Title: add surgery as well.
Response: As requested, this content has been modified. (see page 1, line 4)

2. The abstract is somewhat repetitious and does not include important data of the study.
Response: Indeed, we also found that there is repetition between the abstract and discussion sections. We are very grateful for the guidance of the reviewers, and therefore have made cuts to the content in the discussion section. (see Discussion). Additionally, the main focus of the article is to highlight that immunotherapy is safe and effective in the treatment of thymic carcinoma, which is emphasized in the conclusion section.

3. Introduction: should be better structured.
Response: As requested， this content has been modified. (see page 4, lines 101-108)

Methods:
4. The dose of chemotherapy, PD-1 inhibitors, should be given.
Response: We appreciate the reviewer's more accurate description. We have supplemented

detailed information on chemotherapy drugs. (see page 6， lines145-146, page7 lines 198-199)

5. Some details of surgery should be included.

Response: As suggested, we have supplemented surgical details. (see page 6， lines155-169, page7 lines 208-209)

6. Did the patients receive chemotherapy after surgery or any other treatment?

Response: We appreciate the reviewer's more accurate description. We have added specific details regarding postoperative adjuvant therapy. (see page 6， lines165-166, page 8 lines 211-212)

7. Results: The lab results regarding the function of the liver, kidney, and heart (ECG) – at least the most characteristic parameter -should be included to provide data for comparison to other cases regarding unwanted side effects of treatments.

Response: We appreciate the reviewer's more accurate description. As suggested, this content has been modified (see page 6, lines 177, see page 7, lines 183-184, 188, page 8, lines 222)

8. Tumor shrinkage was observed in “all patients” should be: “both”

Response: As requested， this content has been modified. (see page 3， line 65)

9. Postoperative pathological examinations revealed no residual tumor cells, indicating complete pathological remission”. Was it again a biopsy taken? What does it mean “examination”?

Response: We apologize for any misunderstanding caused by our spelling mistake. There is a grammatical error in the pathological examination, which actually refers to the pathological results of the surgical specimen, without additional examinations beyond pathology. As requested， this content has been modified. (see page 3, lines 66, page 6, lines 161)

10. What does it exactly mean: complete pathological remission?

Response: Complete pathological response is the standard for evaluating the efficacy of preoperative treatment, commonly used in breast cancer, non-small cell lung cancer, esophageal cancer, etc. The diagnostic criteria are as follows: after treatment in the primary tumor area, there are no residual tumor cells in the surgical specimen. If lymph node clearance is required, then the absence of residual cancer cells in the lymph nodes must also be met in order to diagnose complete pathological response. In the past, achieving complete pathological response was difficult in thymic cancer using radiotherapy and chemotherapy, but it is more achievable after immunotherapy.

11. Be specific regarding the histological findings.

Response: As requested, this content has been modified.（page20, lines 592-594, page21, lines 601-603）

12. What is the evidence for this statement: „12 months post-surgery demonstrated no evidence of tumor recurrence or metastasis”?

Response: We are very grateful for the reviewers' suggestions. As requested, this content has been modified. (see page 6, lines167-169, page8 lines 211-214)

13. Were the patients followed up with CT or other imaging examinations after surgery and after 12 months?

Response: As requested, this content has been modified. (see page 6, lines167-169, page8 lines 211-214)

14. Discussion: should be better structured, and subheadings should be included.

Response: As requested, this content has been modified. (see Discussion)

15. What is the average survival of thymoma cancer according to the literature? Some data indicate that it is about 4.5 years long. The present study followed the two cases for 12 months; thus, one cannot foresee the long-range survival, and differentiate between present treatment vs. previous treatments.

Response: We are deeply appreciative of the expert inquiries posed by the reviewers. Indeed, the follow-up period reported in our study was relatively short, allowing visibility only into the short-term therapeutic effects. Our reporting is predicated on the fact that many cancer patients are diagnosed at an advanced stage, where there is a lack of effective treatment options, and achieving a complete pathologic response solely through radiochemotherapy is rare. Therefore, we highlight two case reports of patients who, following immunotherapy and subsequent surgery, achieved complete pathological remission. We hope to offer these case reports as a potentially new and referential treatment paradigm for patients with advanced-stage thymic carcinoma.

16. It is somewhat unclear why in the Introduction and Discussion the authors emphasize the differences between malignant thymoma and thymic squamous carcinoma when both patients had stage III–IV squamous thymic carcinoma. Mechanistic differences of thymoma and thymic cancer should be better described, if possible because the authors try to use this to explain differences in survival and the basis of therapy. Also, the authors emphasize that it is crucial to differentiate between type B and type C thymoma, yet the treatments were the same in these two cases.

Response: We offer our sincere apologies for any confusion this issue may have caused. To clarify: indeed, the two cases of thymic carcinoma were treated with the same therapeutic interventions. Our primary objective was to elucidate the main distinction between thymic carcinoma and thymoma. Thymic carcinoma is characterized by the absence of lymphocytes, whereas type B3 thymoma contains few or no lymphocytes. It is this sparse lymphocytic presence that, following immunotherapy, may become excessively activated, leading to severe autoimmune damage. Therefore, based on our report, the likelihood of thymic carcinoma patients experiencing severe immune-related adverse events post-immunotherapy is low, which is a fundamental difference from thymoma patients who are at a high risk of such adverse events after immunotherapy. Through our findings, we hope to guide the differentiation between type B thymomas and type C thymic carcinomas in the selection of immunotherapy, as indicated in page 10, lines 297-306.

17. The authors perhaps should incorporate the findings of previous publications in their manuscript which would help to better appreciate their findings.

1) (Kameron A. Kooshesh: N Engl J Med 2023;389:406-17. DOI: 10.1056/NEJMoa2302892
2) Naomi Taylor, DOI: 10.1056/NEJMe2306576 n engl j med 389;5 nejm.org August 3, 2023.
3) Covid-19 vaccines elicit effective IgG responses in an elderly thymus cancer patient with chemotherapy HUMAN VACCINES & IMMUNOTHERAPEUTICS 2023, VOL. 19, NO. 1, 2188035 https://doi.org/10.1080/21645515.2023.2188035
4) Letter to Editor 2017 NRITLD, National Research Institute of Tuberculosis and Lung Disease, Iran ISSN: 1735-0344 Tanaffos 2017; 16 (3): 173-174.
5) Liu S, Ma G, Wang H, Yu G, Chen J, Song W. Severe cardiotoxicity in 2 patients with thymoma receiving immune checkpoint inhibitor therapy: A case report. Medicine 2022;101:46(e31873).
6) Palmieri: NEJM Brief Report Volume 336 Number 4. 263-265
7) Cancers 2023, 15, 4018. https://doi.org/10.3390/cancers15164018

Response: We are very grateful for the references provided by the reviewers, and we have read them all.

18. The histological images should be presented with more explanations, regarding cell types, which should be better indicated, perhaps with arrows.

Response: As requested, this content has been modified.（page20, lines 592-594, page21, lines 601-603）

19. What does it mean: improved efficacy and higher safety? Compared to what?

Response： As requested, this content has been modified.（page2 lines 37 ）

20. 202-209 section: pertinent references should be included.

Response: As requested, this content has been modified.（page7 lines 202-204 ）

Reviewer C

Thank you for your valuable comments on this paper. For your questions, our specific responses and modifications are as follows:

In this paper, the authors reported 2 cases of thymic carcinoma in complete pathological remission achieved by neoadjuvant therapy with a PD-1 inhibitor plus chemotherapy. Although I think this is a valuable case report, there are still several concerns as follows.

1. The multitargeted kinase inhibitor lenvatinib has been approved in Japan for patients with unresectable thymic carcinoma based on the positive result of the REMORA trial (Sato J, et al. Lancet Oncol. 2020;21:843-850), and several papers showing the clinical efficacy of lenvatinib have been published. The authors should touch on the topic in Introduction section.

Response: We are very grateful for the reviewers' suggestions. As suggested, this content has been modified.（see page 4，lines92-94）

2. In both cases, Masaoka-Koga stages and best overall responses according to RECIST by ICI

with chemotherapy should be described in Case presentation section and Table 1.
Response: We appreciate the reviewer's more accurate description. We have submitted detailed Masaoka-Koga stages （see page 5，lines140-141, page 7 lines 195） and supplemented corresponding content for RECIST evaluation after treatment（see page 6，lines150-152, page 7 lines 202-204）. We have also supplemented the Masaoka-Koga stages in Table 1. （see page 19 lines 574 ）

3. The authors should describe the drug name of immune checkpoint inhibitors (ICI) in both cases in Case presentation section.
Response: We appreciate the reviewer's more accurate description. We have supplemented detailed information on chemotherapy drugs and immune checkpoint inhibitors.（see page 6，lines145-146, page7 lines 198-199 ）

4. Table 3 is difficult to follow and should be more simplified. It is better to present CTCAE grades and time (day) of onset after initiation of ICI plus chemotherapy for each AE in both cases.
Response: As suggested, this content has been modified（see page 19-20 lines 581 ）.

5. The authors are encouraged to provide appropriate references with careful attention. For example, there are several inappropriate quotations in the manuscript as follows:
a) Lines 80-83: Reference 2 is written in Chinese. The authors should provide appropriate references for this sentence. I suggest to take a look at a review paper by Marx A (J Thorac Oncol. 2022;17:200-213).
Response: First and foremost, I would like to extend my sincerest apologies for our improper citations, and I am also very grateful for the peer reviewer’s professional recommendations. As suggested, this content has been modified.（see page 16， lines478-480）

b) Lines 117-120: The references (References 13 and 14) seem inappropriate and other references should be cited for this sentence.
Response: As suggested, this content has been modified（see page5， lines,125-126, page 17,lines 519-527 ）

c) Lines 160-162: The authors should provide a reference for the guideline of irAE management.
Response: As suggested, this content has been modified（see page 6， lines,176-177 ）.

d) Lines 210-212: This reference (Case report) is not appropriate for this sentence describing the difference in characteristics between thymic carcinoma and high-grade thymoma.
Response: As suggested, this content has been modified（see page 17， lines,519-520 ）.

e) Lines 215-216: The authors described a lower familial predisposition of thymic carcinoma compared to thymoma in this sentence, but it seems to me that no detailed descriptions are found in Reference 17.
Response: We sincerely apologize for the inappropriate citation of the reference. Therefore, following the suggestion, we have removed the relevant content and reference. （see page 8，

lines,237-238)