

Dear Editor,

Thank you very much for your letter and advice. We have read the comments about our manuscript (Manuscript NO.: 70089, Case Report, World Journal of Clinical Cases) carefully and would like to revise the manuscript, and to re-submit for your consideration. We have addressed the comments raised by reviewers, and point by point responses to the reviewers' comments are listed below this letter.

We hope that the revised version of the manuscript is now acceptable for publication in your journal. Please do not hesitate to contact us with any further questions or recommendations. We look forward to hearing from you soon.

With best wishes,

Yours sincerely,

Ying Lin

Department of Dermatology, The Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou 510120, Guangdong Province, China & Guangdong Provincial Key laboratory of Chinese Medicine for Prevention and Treatment of Refractory Chronic Diseases, Guangzhou 510120, Guangdong Province, China.

E-mail: lin19791226@gzucm.edu.cn

Reviewer #1:

1. Please mention the rationale for choosing the therapy as the usual therapy is Sorafenib.

Answer: Thank you for your suggestion. We have added the rationale for choosing the therapy in the "DISCUSSION" sections as follow: Lenvatinib is an antiangiogenic TKI that is widely used in multiple solid tumors[5]. Both lenvatinib and sorafenib are recommended as the first-line treatment for unresectable hepatocellular carcinoma in the guidelines[15]. In a global randomized phase 3 trial, lenvatinib was demonstrated to be non-inferior to sorafenib for overall survival, and it led to greater improvements in progression-free survival, time to progression, objective response and quality-of-life assessments compared with sorafenib[16]. In addition, a synergistic effect has been found between lenvatinib and immune checkpoint inhibitors[6]. The combination of lenvatinib/pembrolizumab is promising in several solid tumors, such as endometrial, lung, hepatocellular and gastrointestinal malignancies[5]. Thus, the patient received combination therapy with toripalimab and lenvatinib.

2. Is the same side effect reported in any cancer condition?

Answer: Thank you for your suggestion. We have searched the pubmed and we didn't find the same side effect reported in any cancer condition. We have revised the sentences in the "DISCUSSION" sections as follow: "Toripalimab was introduced into practice in recent years and widely adopted, especially in China, while no cases of TEN associated with toripalimab have been reported in association with any cancer condition." & "SJS/TEN induced by TKIs is rather rare, and no case of TEN associated

with lenvatinib has been reported in association with any cancer condition. However, we are the first group to report TEN, a grade 4 toxicity, after combination therapy with a PD-1 inhibitor and lenvatinib. Since this was a single case, there is still not sufficient evidence to conclude that combination therapy with a PD-1 inhibitor and lenvatinib increases the risk of TEN compared with a PD-1 inhibitor alone.”

3. have the patient look into only person.

Answer: Thank you for your suggestion. But we apologize that we are unsure of the exact meaning of this question. The patient was treated in our hospital (The Second Affiliated Hospital of Guangzhou University of Chinese Medicine) from the beginning. He received inpatient care for toxic epidermal necrolysis (TEN) in Department of Dermatology. And metastatic liver cancer was managed in Oncology Department, Department of Radiation, and Intervention Department. Please do not hesitate to contact us with any further questions or recommendations.

4. Ethical clearance no is needed as suggested by the journal.

Answer: Thank you for your suggestion. The study was reviewed by Ethics Committee of Guangdong Provincial Hospital of Chinese Medicine. And Ethical clearance No. is G2022-01. The Approval Notice was upload on the system as “70089-Supplementary Material”.

5. I have found some technical errors with the file eg: some words are combined without any separation.may be it is software issue. Please correct it.

Answer: Thank you for your suggestion. The English language has been optimized throughout the manuscript and revised according to your constructive criticisms. The re-editing language certificate was upload on the system as “70089-Language certificate”.

Reviewer #2:

Thank you authors for submitting your manuscript to The World Journal of Clinical Cases. It is a written article and adds information to the existing literature.

Answer: Thank you for your suggestion. We hope that the revised version of the manuscript is now acceptable for publication in the journal.

Science editor:

This case is of guiding value, please mention the rationale for choosing the therapy as the usual therapy is Sorafenib.

Answer: Thank you for your suggestion. We have added the rationale for choosing the therapy in the “DISCUSSION” sections as follow: Lenvatinib is an antiangiogenic TKI that is widely used in multiple solid tumors[5]. Both lenvatinib and sorafenib are recommended as the first-line treatment for unresectable hepatocellular carcinoma in the guidelines[15]. In a global randomized phase 3 trial, lenvatinib was demonstrated to be non-inferior to sorafenib for overall survival, and it led to greater improvements in progression-free survival, time to progression, objective response and quality-of-life

assessments compared with sorafenib[16]. In addition, a synergistic effect has been found between lenvatinib and immune checkpoint inhibitors[6]. The combination of lenvatinib/pembrolizumab is promising in several solid tumors, such as endometrial, lung, hepatocellular and gastrointestinal malignancies[5]. Thus, the patient received combination therapy with toripalimab and lenvatinib.

Company editor-in-chief:

1.Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Answer: Thank you for your suggestion. The original figures were arranged by PowerPoint and the document was upload on the system as “70089-Figures”.

2.Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Answer: Thank you for your suggestion. The approved grant application form(s) was upload on the system as “70089-Grant application form(s)”.