

Dear Editor Wang,

Thank you very much for your decision letter and advice on our manuscript (Manuscript 81808) with the revised title, “Metachronous urothelial carcinomas in the renal pelvis, bladder, and urethra: a case report and literature review”. We also thank the editor and reviewers for their constructive comments and suggestions. We revised the manuscript accordingly, and all amendments are indicated in red in the revised manuscript. In addition, our point-by-point responses to all comments are listed below this letter.

The entire manuscript was also edited and proofread by *Medjaden Inc.*.

We hope that our revised manuscript is now acceptable for publication in your journal and we look forward to hearing from you soon.

With best wishes,

Yours sincerely,

Fa Sun

Email: sfgmc@sina.com

Phone: 0851-28204214

First of all, we would like to express our sincere gratitude to the reviewers for their constructive and positive comments.

Response to the 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.

Response: Thank you for this comment. We prepared and arranged all figures using PowerPoint so that all figures and associated text can be reprocessed by the editor.

2. Please check and confirm whether the figures are original. If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022.

Response: Thank you for this comment. All the figures used in the paper are original. We added the required copyright information to the bottom right-hand side of all PowerPoint figures.

3. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript.

Response: Thank you for this constructive comment. We added text that highlights recent similar case reports of urothelial carcinoma (UC) and the management of upper urinary tract UC (UTUC).

4. To this end, authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under

preparation/peer-review/revision.

Response: Thank you for your kind recommendation. We have used the new Reference Citation Analysis tool and found it very helpful and easy to use. We plan to employ this tool in future studies.

Response to Reviewer 1:

1. This case report is generally well-written. However, it requires deep language and style polishing.

Response: Thank you for your positive comments. We sent our revised manuscript to the professional English language editing company that you recommended. We hope the language and style of the revised manuscript are now acceptable.

2. Is it really a case of "successive carcinomas" or a case of metachronous cancer?

Please, consider to change the title, if applicable.

Response: Thank you for this constructive comment. We reviewed the usage of “successive” and “metachronous” in the literature and believe that “metachronous” is the more suitable term. Thus, we changed the title to “Metachronous urothelial carcinoma in the renal pelvis, bladder, and urethra: a case report and literature review” and revised the text accordingly.

3. I would recommend to add more details on the specificity/originality of the described case (what a reader can learn from the described case? what conclusion(s) can be made based on the described? and whether some change in the standard clinical practice should be made or at least discussed), instead of repeating the data of the case once again.

Response: Thank you for these constructive comments. We added more details in the “Case Description” section by including information regarding the patient’s medical history, blood biochemistry, chest X-ray, cystoscopy, and biopsy results. We also added recommendations in the Discussion regarding the usage of adjuvant Bacillus

Calmette-Guérin (BCG) immunotherapy for patients with upper UTUC.

4. In this part, please, add the details of the possible reasons of such an unusual localization and re-appearance (genetic? viral? etc) if possible.

Response: Thank you for this constructive comment. We agree that it would be interesting to have more details regarding the possible reasons for the unusual localization and re-appearance of the lesions. Unfortunately, due to the lack of analysis of oncogenes, we do not have information regarding the underlying molecular mechanism. However, because upper UTUC has the properties of multifocality and downstream seeding, this certainly played a role in the re-appearance of the lesion.

5. Please, consider to change the Conclusion, as the current one is self-evident and does not require the publication of a case-report.

Response: Thank you for your constructive comment. We changed the Conclusion and stressed that upper UTUC is prone to seeding and recurrence, thus making it important to employ adjuvant instillation of BCG.

6. Ethical statement: according to the described, it was not a study, and the subject was treated according to standards of care with the real life influence. The data were collected retrospectively. The subject could provide an informed consent to use the data in the scientific purposes and publication of the data of his examination or even no specific consent. Please, check the Ethics statement section.

Response: Thank you for the thoughtful comment. We received informed consent from the subject to use the data for scientific purposes and publication of the data of his examination. We will upload these materials when submitting our revised manuscript.