Author's response to reviews

Title: Application of contrast-enhanced ultrasonography for Large cell neuroendocrine carcinoma in urinary bladder: a case report

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Dear Reviewers and Editors,

Thank you very much for your comments on and suggestions for our manuscript BMIM-D-20-00061R2, entitled "Application of contrast-enhanced ultrasonography for Large cell neuroendocrine carcinoma in urinary bladder: a case report" which are very valuable and have helped us revise and improve our manuscript. We appreciate all of your work on our manuscript. We have carefully studied your comments and corrected our manuscript accordingly. We hope this version of the manuscript meets your approval. The main corrections in the paper and the response to the editor and reviewers are as follows:

Response to Editor

Interesting case. Presentation and Discussion are overall OK. Please, check carefully for English language (there are several typos, e.g. at the beginning of case presentation in the main text), and provide comments to reviewer's # 3 observations.
Response: Thank you very much for your comments. We have turned to American Journal Experts to correct the mistakes in language editing and choice of words. The editorial certificate has been uploaded as an attachment.

Response to Reviewer 1:

This paper shows role of US and CEUS in large cell neuroendocrine carcinoma (LCNEC) of the urinary bladder with anato-pathologic correlation
The theme is not novel, but it is very rare. In literature, there are no studies about the role of CEUS in diagnosis of this type of tumor.
The manuscript is nicely written, and the content is simple and easy understanding.
Response: Thank you very much for approval.

Response to Reviewer 2:

Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format. Please overwrite this text when adding your comments to the authors.
Response: Thank you very much for approval.

Response to Reviewer 3:

1- Page (31-39) I advise this sentence to be shortened- However in clinical practice, CT and MRI scans are expensive, not widely available and have an inherent risk of adverse reactions associated with-----
Response: Thank you very much for your comments. We have revised the text to” However, CT and MRI scan are expensive and sometimes unsafe because of adverse reactions associated with using iodine as a contrast medium”

2- Following this please add that sometimes patients may have high urea and creatinine levels and may be in early stages of kidney disease and may bot be able to tolerate CT and MRI contrast media and US may be useful in this scenario as well.
Response: Thank you very much for your comments. Your suggestion is very helpful. We have added this sentence ” In addition, some patients with high urea and creatine levels or in early stages of kidney disease may not be able to tolerate CT and MRI contrast medium and US may be useful in this scenario as well.” to the second paragraph of the discussion.

3- page 8-line 37 Guo et al “ slow wash out time " contradicts the fast wash out observed in the case study please clarify this.
Response: Thank you very much for your comments. we further check out our paper and revise this mistake.

4- Is it possible to discriminate large cell neuroendocrine bladder cancer from other common bladder tumors especially transitional cell carcinoma of the bladder. TCC of the bladder or squamous type's features are the most studied and variance of LCNE tumor from this type of tumor need to be discussed in the discussion as well regarding US features and CEUS features as well.
Response: Thank you very much for your comments. We added the discussion of differential diagnosis in the fifth paragraph of discussion.

5- In the presence of a bladder tumor, ureterovesical -ureteric involvement and presence of hyrdonephrosis are also important and the need to evaluate there parametersvshould be mentioned as well.
Response: Thank you very much for your suggestion. We added “No invasion of the trigone of bladder and bilateral hydrenephrosis was observed.” in the second paragraph of the Case presentation.