

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Female genital tract metastasis of lung adenocarcinoma with EGFR mutations: 2 case reports and review of literature" (ID: 45991). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in highlight in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Reviewer #1:

1. Response to comment: Page 7: A description of the abbreviations should be written. i.e. CDX2(-), PSX8(-), Ki67

Response: We are very sorry for our mistake, The word "PSX" needs to be corrected for "PAX", which are marked in highlight in page3 and page8. PAX is the abbreviation of "paired-box 8", which is an important marker for the diagnosis of ovarian diagnosis.

As reviewer suggested that, we make a supplement of abbreviations in page 17, as follows, " Abbreviations: EGFR epidermal growth factor receptor; TKI tyrosine kinase inhibitor; CT computed tomography; PET-CT positron emission tomography-computed tomography; TTF thyroid transcription factor-1; CK cytokeratin; CDX2 caudal-related homeobox 2; PAX8 paired-box 8".

2. Response to comment: Page 4, 6: The normal values of the tests should be given. Carcinoembryonic antigen: 1.5 ng/ml, which was negative. Carcinoembryonic antigen: 4.4 ng/ml, Tumor-associated carbohydrate antigen 125: 42.9U/ml.

Response: We are very sorry for our negligence of the normal values. We make it supplemented as follows: Page4: Carcinoembryonic antigen: 1.5 ng/ml (0-5ng/mL), which was negative. Page 7: Carcinoembryonic antigen: 4.4 ng/ml (0-5ng/mL), tumor-associated carbohydrate antigen 125: 42.9U/ml (0-35U/mL).

3. Response to comment: Page 9, second paragraph: Reference number should be given. In certain situations, liquid biopsy could be an essential tool for clinicians, especially for patients who cannot undergo invasive diagnostic procedures [que].

Response: We are very sorry for our incorrect writing, and the reference number is [13], which has been marked in the highlight.

Special thanks to you for your good comments.

Responds to the editor's comments:

1. Page1, the running title "Uncommon Site Metastasis of Lung Adenocarcinoma" was added.
2. Page2, "Supportive foundations: This research was supported by the National Natural Science Foundation of China [NO.81670017]." was added.
"CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016)." Was added.

“Telephone: +86 571 872 36876 Fax: +86 571 872 36877” was added.

3. Page3-4, “Core tip: The female genital tract is an uncommon site of involvement for extra-genital malignancies. Ovarian metastases have been described as disseminations of lung adenocarcinoma; rare cases of secondary localizations in cervix, adnexa and vagina have also been reported in the literature. Here, we report two cases of advanced lung adenocarcinoma with female genital tract metastasis. The initial tumor site should be considered when both pulmonary and female genital tract neoplasms exist. Immunohistochemistry and gene mutational testing have greatly helped in locating the initial tumor site.” Was added.

“Audio core tip” will be uploaded.

4. Page4, we have made revision of all the reference numbers according to the editor’s comments that “The reference numbers should be superscripted in square brackets at the end of the sentence” and marked in highlight.
5. Page 10-12, reference “ [13] Hiley CT, Le Quesne J, Santis G, Sharpe R, de Castro DG, Middleton G, et al. Challenges in molecular testing in non-small-cell lung cancer patients with advanced disease. LANCET. 2016 2016-09-03;388(10048):1002-11 [PMID: 27598680 DOI: 10.1016/S0140-6736(16)31340-X]” was added ,thus the original reference numbers 13 and 14 were extended to 14 and 15.
6. Page 11-14, PubMed citation numbers and DOI citation were added and all authors of the references were added, which were marked in highlight.
7. Page 14-17, Original and separated figures were added and uploaded.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked in red in revised paper.

We appreciate for Editors/Reviewers’ warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.