NANCHANG UNIVERSITY
The Fourth Affiliated Hospital

HUAN DENG, M.D., PH.D.
Professor of Pathology
Chief, Department of Pathology
Chief, Molecular Medicine and Genetics Center
133 South Guangchang Road
Nanchang, Jiangxi, China 330003
Tel: + (86) 791 87022537
Fax: + (86) 791 87022537
E-mail: *beandeng@ncu.edu.cn*

November 16th, 2022

Re: Revision of "Fat-poor renal angiomyolipoma with prominent cystic degeneration: a case report" *World Journal of Clinical Cases* Manuscript NO: 80121.

Dear Professor Wang,

Thanks very much for your kind letter from November 4, 2022 and your note that our manuscript "may be acceptable for publication after appropriate revision".

We have reviewed the comments carefully and have now addressed all of the reviewers' and editors' concerns that were raised.

Below we have included a point-by-point response to all these concerns.

Editors' concerns:

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: Thanks for the suggestion. We have uploaded all original figures using PowerPoint.

2. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). 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: Thanks for your suggestion. This has now been done.

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

Response: Thanks for your suggestion. The covers of every funding have been uploaded.

4. 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. To this end, authors are advised to apply a new tool, the RCA.

Response: Thanks for this suggestion. We have expanded the discussion section and cited the latest cutting-edge research results in the diagnosis and treatment of AML (Page 9-11).

Reviewer #1 concerns:

1. In order to improve the quality of the work, I suggest enlarging the size of the arrows in Figure 1.

Response: Thanks for this suggestion. The arrows in Figure 1B and 1D have been enlarged.

2. In addition, in histology microphotographs it is essential to include the magnifications used and/or include a scale.

Response: Thanks for this suggestion. We have added the magnification and scale of Figures 2 and 3.

Reviewer #2 concerns:

1. In the History of Present Illness section, it's not entirely clear why the patient presented. We know he had a renal mass diagnosed 5 years prior and that he had a "fall several months ago." Was the health examination report a clinic visit or imaging? Why was it done? I would recommend describing the story/timeline more clearly.

Response: Thanks for this suggestion. The patient annually received the medical

examination given by his company and was told in 2017 that he had a cystic mass in the left kidney. He fell two months ago. A CT scan of the abdomen at a local hospital showed a growing mass (measured 6 cm in diameter) in the kidney. All health examination reports were imaging. We have revised the History of Present Illness section to ensure a clearer timeline (Page 5, Para 2).

2. In the History of Past Illness section, any clinical signs/symptoms of tuberous sclerosis? Or prior scans/imaging showing sporadic lymphangioleiomyomatosis?

Response: Thanks for your suggestion. There were no clinical signs of tuberous sclerosis such as facial sebaceous adenoma, epilepsy or intelligent impairment and no prior imaging showing sporadic lymphangioleiomyomatosis like pneumothorax, chylous pleural effusions or cystic lung disease. We have supplemented this in the History of Past Illness section (Page 5, Para 3).

3. In the Family History section, would specify in terms of any history of renal masses, renal cell carcinoma, angiomyolipomas, tuberous sclerosis, etc.

Response: Thanks for this suggestion. We have added the sentence to the Family History section (Page 5, Para 4).

4. In the Treatment section, I would elaborate. To my understanding, he underwent laparoscopic cyst deroofing and then biopsy? Was percutaneous biopsy ever considered? Was this approach taken due to high concern of malignant transformation? Was radical nephrectomy chosen due to the fact that RCC could not be ruled out? Was partial nephrectomy or nephron-sparing approach ever considered?

Response: Thanks for your suggestion. The patient initially underwent laparoscopic renal cyst deroofing due to the diagnosis of left renal cyst, and intraoperative rapid paraffin examination was performed in order to further confirm the nature of the tumor. Percutaneous biopsy of benign tumors can show the characteristics of nuclear atypia and pleomorphism, which are easy to be misdiagnosed as malignant tumors, and it may cause bleeding of the hemorrhagic cyst. Therefore, it was not considered. Pathological examination showed that the possibility of malignancy was high, so the patient received radical nephrectomy. We have modified the Treatment section to ensure that the reasons for operation choice are more clearly stated (Page 6, Para 4).

5. In the Outcome/Follow Up section, was he evaluated for tuberous sclerosis complex with genetic testing or examinations otherwise?

Response: Thanks for your suggestion. ECG and chest X-ray examination were performed half a year after operation, and no signs of tuberous sclerosis were found. We have edited the Outcome/Follow Up section (Page 7, Para 4).

6. Overall I think the discussion section is quite good. I would elaborate on how sporadic AMLs are typically managed and what made this case interesting/unique.

Response: Thanks for your kind suggestion. We have added three new paragraph to elaborate on the clinical management and treatment of AML (Pages 10-11). AML with large cystic degeneration is extremely rare. In the new paragraph, we have explained the particularity of this case in detail (Page 11, Para 4).

7. In the conclusion, in the text "However, in this case, we should note that when faced with a large cystic mass of the kidney, we cannot rule out the possibility of AML"; did you mean to say rule out the possibility of RCC?

Response: Thanks for this suggestion. To our knowledge, AML with cystic degeneration has rarely been documented and accounts for less than 1% of RAML. In this case, the imaging examination did not support AML firstly. The correct diagnosis was finally established by postoperative histopathological and IHC examinations. Therefore, we hope to show that the possibility of AML should be considered basing on the cystic degeneration of a renal mass.

8. There are some ways the writing could be improved as well e.g. in the core tip can just summarize and not necessarily say too much about the case/patient per se.

Response: Thanks for this suggestion. We have revised the core tip, reducing the description of the case itself and summarizing the core ideas more (Page 4, Para 1).

Reviewer #3 concerns:

1. A state of the art section should be included.

Response: Thanks for this suggestion. See above. We have cited the latest cutting-edge

research results to support the Discussion section (Page 9-11).

2. The discussion should be expanded and improved so that the work presented is compared with other similar ones. Establishing the limitations and advantages. References should be expanded.

Response: Thanks for your suggestion. We have supplemented the Discussion section and introduced the differential diagnosis (Page 9-10) and clinical management (Page 10-11) of AML in more details. At the same time, we have added an additional paragraph to explain the limitations and advantages of this report (Page 11, Para 4). Eighteen new references have been cited (#17-21, 34-46).

3. In the conclusion, the scientific contribution must be synthesized and a set of lines of future work must be established.

Response: Thanks for this suggestion. We have supplemented the Conclusion section and proposed a more detailed diagnosis management strategy for AML (Page 12, Para 1).

Reviewer #4 concerns:

1. The histological figures (Figure 2 and 3) are inadequate and must be changed by higher quality figures with a perfect resolution.

Response: Thanks for this suggestion. We have uploaded new Figure 2 and 3 with high resolution.

2. The authors should add a figure illustrating the macroscopic aspect of the tumor.

Response: Thank you for this suggestion. Unfortunately, the original macroscopic pictures were not retained as it was not initially considered a tumor.

3. The references are not up-to-date.

Response: Thanks for this suggestion. See above. We have cited eighteen new references. The proportion of literature in recent five years has exceeded 30%.

4. The style, language and grammar require minor revision.

Response: Thank you for this suggestion. We have added more details to the manuscript

and then revised it carefully with the help of Springer Nature Language Editing Service.

5. This manuscript does not add anything new to the medical literature.

Response: Thank you for this suggestion. RAML is the most common tumor of the kidney. The cystic degeneration of this tumor may lead to misdiagnosis as common cystic diseases, resulting in delays in treatments. Although only a few cases report this rare subtype of RAML, the cystic feature should be included in the differential diagnosis of RAML.

Revision reviewer#1 concerns:

As indicated in the text, a few grammatical revisions are needed. With those corrections, I think this can be accepted for publication.

Response: Thanks for your suggestion. All grammatical revisions indicated in the text have been finished.

Revision reviewer#2 concerns:

The paper can be accepted in current form

Response: Thank you for your comments.

We hope that you find our paper is now acceptable for publication.

Sincerely yours,

Huan Deng, M. D., Ph. D.

Chief, Department of Pathology

Chief, Molecular Medicine and Genetics Center

The Fourth Affiliated Hospital of Nanchang University

Chief, Cancer Immunology Institute

Nanchang University

E-mail: beandeng@ncu.edu.cn

Tel: +86-791-87022537

Fax: +86-791-87022537