

Dear Editors:

Thank you very much for your letter and advice. We have revised the manuscript, and would like to re-submit it for your consideration. We have addressed the comments raised by the reviewers, and the amendments are highlighted in red in the revised manuscript. 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.

I look forward to hearing from you soon.

With best wishes,

Yours sincerely,

Yibao Wang, MD, Professor

Corresponding author

We would like to express our sincere thanks to the reviewers for the constructive and positive comments.

## Replies to Reviewer 1

### Specific Comments

1. Page 2, Introduction section. Please spell Renal Cell Carcinoma in full before using its abbreviation in the text. Having used the abbreviation within the abstract is not sufficient reason to use it without full spelling the first time it appears within the main text.

**Answer:** Correction has been made in the revised version. (page 4, introduction section, paragraph 1, line 1).

2. The overall quality of the English text is good. Nevertheless I would like to recommend that the manuscript be revised by a native English speaker to amend a few details. For instance: P2, introduction section: "Tumors originating from the clivus are rare: chordomas, which are the most frequent tumor of this region...". I believe this sentence could be improved: Tumors originating primarily in the clivus region are very rare. Chordomas, which are the most frequent tumor affecting that region...".

**Answer:** The sentence mentioned has been improved in the revised version. (page 4, introduction section, paragraph 1, line 7). The manuscript has been revised by a professional language editing company, and certificate of editing has been sent to the editors.

3. Because not all renal cell carcinomas are clear cell carcinomas, the authors should refer specifically to Renal Clear Cell Carcinomas (RCCC) throughout the text and not simply to Renal Cell Carcinomas. See Delahunt & Eble, Clin Lab Med 2005; 25(2):231-246 ([https://www.labmed.theclinics.com/article/S0272-2712\(05\)00007-7/abstract](https://www.labmed.theclinics.com/article/S0272-2712(05)00007-7/abstract))

**Answer:** The elucidation of biology research to RCCC has led to the interest in and success of targeted therapy for this subtype of RCC. In other respects such as prognosis and other treatments, renal cell carcinomas in general are described in most studies. Several parts throughout the text have been modified to refer specifically to RCCC, and relevant content of renal clear cell carcinomas has been added in the revised version.

(1) "renal cell carcinoma" has been modified to "renal clear cell carcinoma"

in the revised version (page 1, title; page 3, abstract section, paragraph 1, line 1; page 3, abstract section, paragraph 1, line 11; page 3, key words; page 3, core tip section, paragraph 1, line 1; page 4, introduction section, paragraph 1, line 13; page 6, discussion section, paragraph 1, line 3; page 6, discussion section, paragraph 1, line 8; page 6, discussion section, paragraph 2, line 12; page 9, discussion section, paragraph 6, line 14; page 9, discussion section, paragraph 6, line 17; page 20, table 1 title).

(2) Several sentences related to RCCC have been added in the revised version.(page 4, introduction section, paragraph 1, line 3; page 8, discussion section, paragraph 6, line 10).

4. I would like to suggest the authors to use arrows to show specific important details within figures.

Answer: White arrows have been added in Figure 1, Figure 2, and Figure 4 to show the specific important details in the revised version (page 16, figure 1; page 17, figure 2, page 19, figure 4).

5. Please specify if the literature review encompassed Renal Cell Carcinomas in general or Renal Clear Cell Carcinomas.

Answer: According to the histopathology revealed by the reports, the literature review has been modified that encompasses the cases of clival metastasis specifically from RCCC. 4 case reports of clival metastasis from RCC in general have been removed from the table 1 (page 20, table 1).

6. P7, first paragraph “The possibility of metastatic RCC should be sought when acute cranial neuropathies occurs on a patient presents.” This sentence ends abruptly and is not clear, please double-check the intended message. I also believe that instead of the verb “to seek” the authors should use the verb “to consider”.

Answer: The sentence has been modified as “The possibility of metastatic RCCC should be considered in patients with a clival lesion and cranial neuropathies” and added to the page 6, discussion section, paragraph 2, line 12. The sentence is to conclude the above part.

7. In the abstract the authors describe the treatment approach that they used to help the patient. However there is no mention within the main text besides table 1 about details of the treatment of the patient, complications of the treatment and patient outcome. Those pieces of information are very important for the reader because they provide valuable information for clinicians caring for patients with a rare condition. It would be very

interesting to inform readers if the patient survived treatment and what is his likely prognosis, if the developed sequelae from tumor/surgery, if the tumor recurred either locally in the clivus or elsewhere in his body. This should be done within the case report section. Additionally and ideally, a new column could be added to table 1 informing readers about the outcome of the management of the patients described in those case reports that were reviewed.

**Answer:** The patient presented no postoperative complications of the 2 surgeries and discharged home after routine postoperative treatments. The details have been added in the case report section of the revised version (page 5, case report section, paragraph 3, line 5; page 5, case report section, paragraph 3, line 21). Among the case reports reviewed, they rarely described the outcome of every management. Almost no available information can be added in the table 1.

8. Please, transfer the table to a page formatted under landscape mode at the end of the text, in order to increase its readability.

**Answer:** The table has been transferred to a page formatted under landscape mode at the end of the revised version (page 20, table 1).

9. Please, avoid using the word gender in the table to refer to biological sex. Gender is really about a social construct and can be different than biological sex.

**Answer:** Correction has been made in the table 1 (page 20, table 1).

10. The last paragraph of the discussion section deals with the treatment of RCC. Many of its statements do not have a proper reference. E.g. "The benefit of radiotherapy in the treatment of RCC remains unclear and is not recommended. Stereotactic radiotherapy has been shown to be successful in both reducing local symptoms from tumor bulk and stabilization of the growth of metastatic lesions at both cranial and extracranial sites."

**Answer:** The relevant references have been added to the sentence in the revised version (page 8, discussion section, paragraph 6, line 5).

11. There should be at least a paragraph within the discussion section concerning the prognosis of patients with RCC in general and in those with metastases including to the central nervous system.

**Answer:** There are only some studies revealing data on the prognosis of patients with RCC in general and in those with metastases including to the

central nervous system. The paragraph has been added in the revised version and we have provided the relevant content about RCCC in these studies (page 8, paragraph 5).

## Replies to Reviewer 2

### Specific Comments

1. Major remarks The following publications can be included in table 1 or discussed (and the last sentence of introduction would be: "...with few cases previously..."): - Gil Salu <http://www.revistaneurocirugia.com/en-congresos-xxi-congreso-nacional-sociedad-espanola-47-sesion-oncologa-oncology-3252-metstasis-clival-tarda-de-carcinoma-35900-pdf> - Zahra doi: 10.1016/j.ijrobp.2014.05.2016 - Patel [www.triomeetingposters.org/wp-content/uploads/2013/01/009.pdf](http://www.triomeetingposters.org/wp-content/uploads/2013/01/009.pdf) - Ouma doi: 10.1016/j.wneu.2017.09.068 - Campbell doi: 10.1594/ecr2010/C-1347 - Santhosh <http://oncologypro.esmo.org/content/download/125614/2375060/file/2017-ESMO-Preceptorship-I-O-Participant-Clinical-Case-Discussion-Immunotherapy-Advanced-RCC-Santhosh-Kumar-Devadas.pdf> - Neelakantan doi: 10.1016/j.crad.2014.07.010 - Chamoun doi: 10.1227/NEU.0b013e318236a700

Answer: The sentence "...with no more than 9 cases previously ..." has been modified to "Clival metastases from RCCC account for a small proportion of clival tumors, few cases having been reported". The publications mentioned of "METÁSTASIS CLIVAL TARDÍA DE CARCINOMA RENAL DE CÉLULAS CLARAS", "Renal Cell Carcinoma with Metastasis to the Clivus", and "Immunotherapy to the rescue in advanced RCC" have been included in table 1 and discussed in the revised version (page 6, discussion section, paragraph 1, line 2; page 20, table 1).

2. It would be useful for authors of further reviews to know the results of gamma knife treatment and the end of follow-up (date of resubmission) in order to calculate the survival.

Answer: The results of gamma knife and the recent follow-up have been added in the revised version (page 5, case report section, paragraph 3, line 25; page 20, table 1).

3. In table 1 (instead of year of reporting) include which was firstly diagnosed, the clival metastasis or the primary RCC (and the interval between them).

Answer: The column of year of reporting has been removed from the table 1. A new column of first diagnosis and interval between the clival metastasis and the primary RCCC has been added in table 1 (page 20, table 1).

4. Minor remarks Typing errors: Fumino, sunitinib, sorafenib, adrenal gland.

Answer: Corrections have been made in the revised version (page 4, introduction section, paragraph 1, line 6; page 9, discussion section, paragraph 6, line 15,16; page 20, table 1).