Peer Review File

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Reviewer A

I suggest the acceptance after minor reviews and an extensive review of the English language.

1) Please, extensively modify the English language through all the Manuscript, which may strongly limit the citations of the article (example: Line 93 - "All patients recovered well without recurrence…."; it is not scientific English language). The article in this version is difficult to be read and be considered by English/American authors;
Reply: Thanks for reviewer's comment. We are extremely sorry for our poor English. In order for authors to better understand our research, we performed a language polishing. We hope that the revised manuscript could be lucid for all readers.

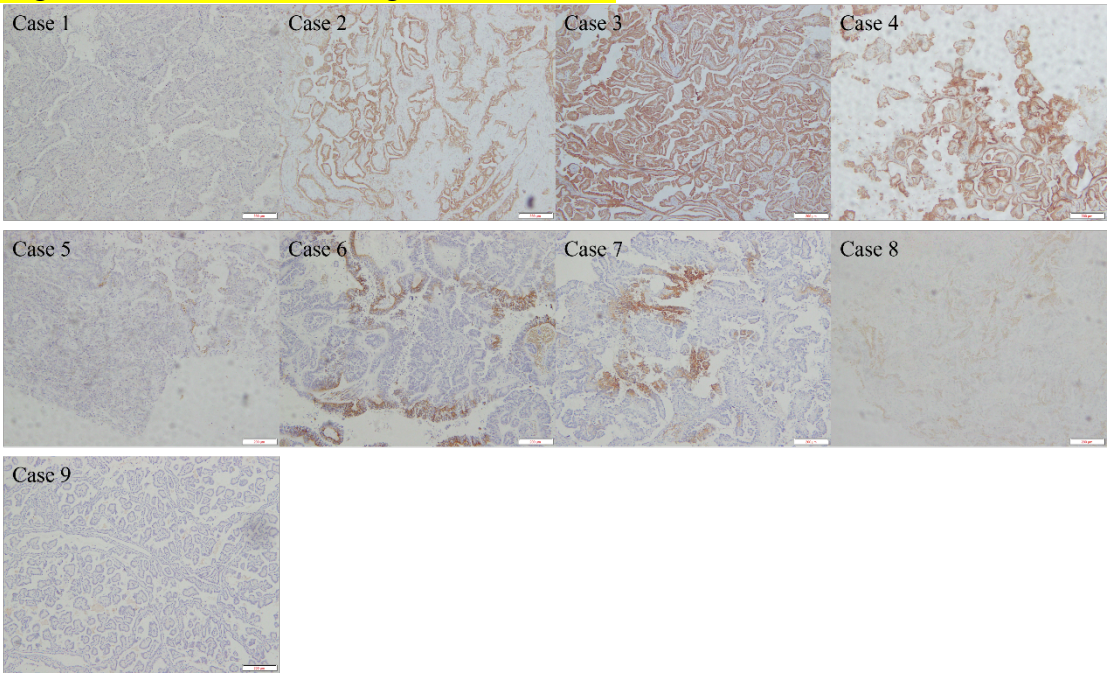
2) Please, adopt the updated terminology of ccPRCT and PRCC in the Manuscript (you could discuss the past division in type 1 and 2 PRCC, but I suggest to shorten the discussion about type 1 and 2 in Introduction, and limit the adoption of this term).
Reply: Thanks for reviewer's comment. We revised the manuscript and shorten the description of type 1 and 2 PRCC in the part of Introduction (see Page 4, line 121-line 133). We reduced the unnecessary use of type 1/2 in the Results, Discussion and Tables (see Page 7, line 223; Page 12, line 392; Table 2). We deleted all the terminology of ccPRCC and only used ccPRCT (see all parts; Table 6).

3) As suggested by the authors, these tumors have eosinophilic cytoplasm and sometimes may not form papillae, thus raising the differential diagnosis with oncocytic tumors. Indeed, for many years the so-called oncocytic PRCCs were thought to be a variant of oncocytic rather than papillary tumors. Besides, considering the frequent central stromal degeneration and shared immunohistochemical features (GATA3 and CK7+, CD117-), these tumors could be in differential diagnosis with low-grade oncocytic tumor (LOT) of the kidney, especially on core biopsy. However, these tumors are finally distinguished by additional morphological, immunohistochemical, and especially molecular features (KRAS in PRNRP and TSC1/TSC2/MTOR in LOT). Please, discuss this relevant point (especially on core biopsy) and refer to the following references (doi: 10.1007/s00428-023-03673-9; doi: doi: 10.1111/his.14816)
Reply: Thanks for reviewer's comment. We supplemented the data of 3 LOTs in the part of results (Table 6) and the discussion of differential diagnosis between PRNRP and LOT (Page 13, line 418-429).

4) Line 388: "There has been a study performing the next-generation sequence on the PRNRPs, while for the tumors with KRAS missense mutation, no extra mutual gene variation was found (28) ting the oncogenesis of PRNRP". Please, split these two points in two sentences, one focused on other than KRAS mutations potentially involved in PRNRPs (BRCA2, etc.) and one on mutations potentially coexisting with KRAS in PRNRP (TP53, BRCA2, etc.). Refer to all the References involved in this topic (not only 28 but above all 14) and modify the Manuscript accordingly.
Reply: Thanks for reviewer's comment. We supplemented the discussion about the various molecular variations of PRNRP and presented our view about the different detecting results (Page 14-15, line 459-470).

5) Are you sure of CA-IX stain? This stain has not been diffusely investigated in PRNRP, but in my personal experience is always completely negative and/or focally positive.

Reply: Thanks for reviewer's comment. We carefully revised the pathological sections of 9 cases and we were sure that our interpretation of CAIX was correct. We provided the photo of CAIX of 9 cases. Based on our experience, most of the positive staining were weak and focal (+~++) which might be low value for the diagnosis of PRNRP.



6) Line 309: "These phenomena indicated that irreversible destruction of nephron might be a nonnegligible reason for the tumorigenesis of PRNRP". Please, remove this confounding and not supported sentence.

Reply: Thanks for reviewer's comment. We removed this sentence.

7) Please discus also the article by Chang HY et al (References 18), where the authors found that type D papillary adenoma could be the same lesions or be along the same spectrum of PRNRP (smaller size and/or the "adenoma variant" of a probably but not surely benign tumor"; in my personal idea, they are the same lesions).

Reply: Thanks for reviewer's comment. We supplied the discussion of type D papillary adenoma in the part of discussion and we agreed that this kind of papillary adenoma were actually the same lesions with PRNRP (Page 10, line 323-326).

Reviewer B

The authors report herein the morphological and immunohistochemical features of a series of 9 patients with papillary renal neoplasm with reverse polarity, along with their KRAS mutational profile.

There are 2 major issues: (1) the language is sometimes poor, hence a thorough language revision is needed, and (2) lack of novelty: although this is still an uncommon entity, an increasing number of such cases is being reported lately, and this study adds no new insight to our knowledge of this entity.

Reply: Thanks for reviewer's comment. We were extremely sorry for our poor English. In order for authors to better understand our research, we performed a language polishing. We hoped that the

revised manuscript could be lucid for all readers. For the second comment, in this study, we slightly expanded the morphological spectrum of the entity (described one case with psammoma body formation) and also used p53, Ki-67 and many immunohistochemical markers of molecularly-defined RCC that had not been used to characterize this entity before. We hoped that this study could be a pragmatic reference for some pathologists and clinicians to understand this disease.