Author’s response to reviews

Title: Corticomedullary mixed tumour resembling a small adrenal gland-involvement of cancer stem cells: case report

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The authors' response letter has been included as a supplementary file.

Editor Comments:
1. Please ensure that you remove the consent form associated with this publication - this compromises patient anonymity. Please also remove additional files referring to conflict of interest disclosures.

We thank the editor for bringing these to our attention. We have removed the consent form and conflict of interest disclosures, respectively.
2. The manuscript submissions to BMC Endocrine Disorders must contain a Declarations section.

Thank you for your reminding. The declarations are prepared in our manuscript (please see declarations section, line 255-277, page 11).

Reviewer 1: Comments

1. There is a recent detailed review of the literature by Michalopoulos et al in Surg Today that should be included both in the introduction and the discussion.

We thank the reviewer for the suggestion. We have added the latest literature review to the background and the discussion (please see background section, line 85-89, page 4 and discussion section, line 126, page 5 to discussion section, line 154, page 6).

2. More bibliographic data would be interesting to be added (see article of Michalopoulos et al).

We have added bibliographic data for interesting reading (please see table 1).

Reviewer 2: Nice case report

Few Concerns.

First. You wrote about a mixed tumor which is actually well defined in "layers". Was is within the nodule, or was not possible to define "tumor nodule" and "normal" adrenal?

In this case you should refer to a synchronous cortico-medullar tumor rather than mixed. You should develop more this point in result and not in discussion as well as move within result the staining part.
We thank the reviewer for bringing this to our attention. Indeed, as you said, our mixed tumor is composed of cortex originated in the mesoderm and medulla originated in the ectoderm. The mixed tumor is in the nodule. Tumor nodule and "normal" adrenal layered clear, well-defined coexistence in the right adrenal capsule (please see the figure below). Our case is an indeed synchronous cortico-medullar tumor. We modify the results and discussion for reflecting the characteristics of synchronization (please see case presentation section, line 113-114, page 5 and discussion section, line 159-162, page 6).

Second. In Conclusion you stated that you "demonstrated" the role of stem cells in the development of this tumor. Have you a different grade of differentiation of these stem cells within your stainings? To better clarify. Starting from the fusiform stem cells, have you different fusiform cells that stained for both markers of cortical and medullary tissue or starting form the very first stem cells, some demonstrated differentiation towards cortical and towards medullary? because otherwise you "made the hypotesis" about the stem cells. I think that a revision would be needed.

Thank you for your professional advice. We hypothesizes that stem cells could involve in the formation of the tumor. The research is a relatively superficial observation. We don’t supply the staining results you mentioned. Further researches should be needed to confirm in the future, such as the staining of different grade of differentiation of cancer stem cells and both markers of cortical and medullary. In order to be more rigorous, we modified the content of the article (please see abstract section, line 59, page 3 and discussion section, line 166, page 6).