Reviewer's report

Title: The identification of H3F3A mutation in Giant Cell Tumour of the Clivus and the histological diagnostic algorithm of other clival lesions permit the differential diagnosis in this location.

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Reviewer: Thomas Barth

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In the MS entitled: "Histone 3.3 mutation is responsible for the rare giant cell tumor of the clivus: implication for diagnosis and treatment the authors have analyzed two giant cell tumors of the clivus regarding the mutational status of H3F3A,-B, IDH1 and-2, and ZN687. They further included immunoistochemical data regarding the mutational antibody G34w and tenascin as well as RANKL.

The MS is interesting regarding the diagnostic aspects of GCT, even though it has the character of a case description.

I can recommend publication in the case the following items are addressed:

1. Authors have to show in a meta-analysis that the clivus is really a rare location by reviewing the literature including all data possible, i.e. data from the Rizzoli Institute etc. They should show (and discuss) what are the main differential diagnosis in this region.

2. The authors cite that they have performed tenascin stainings. However, they do not link the data to the published data, nor do they discuss or show the tenascin results. Does this help to distinguish GCT from other giant cell rich lesions or lesions in general of the clivus?

3. The authors have analyzed H3F3-B, IDH1 and-2, and ZN687. However, they do not discuss why they have done this and what are the results regarding the sequencing of these regions? What is the rational for this approach, does this help to exclude other giant cell rich tumors, further sarcomas?
4. I suggest to generate to an diagnostic algorithm including histology for the most frequent lesions of the clivus region including metastases, chordomas, further types of sarcomas etc.

5. What is the clinical course of the disease in the two patients? Are they free of disease? Further therapy?

6. Change the title. The authors do not show that the mutation is responsible for this tumor. They detect the mutation in the tumor, however, this is no proof of principle such as a knock-out/-in experiment. A suggestions is: GCT of the clivus as a rare entity in this location

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.
Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.
Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.
Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
Not relevant to this manuscript

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Please indicate the quality of language in the manuscript:
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