Author’s response to reviews

Title: A case report of an unusual non-mucinous papillary variant of CPAM type 1 with KRAS mutations

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Author’s response to reviews:
Dear Editor(s),

Thank you for considering our manuscript for publication and the reviewers for their valuable comments. Below you will find our responses to the issues raised by the reviewers. Hopefully we have responded appropriately to these comments. We have highlighted the changes in our revised manuscript in yellow. We have also uploaded this response as a Response Letter (Revision Response Letter) as a Supplementary Material. If any further clarification is necessary, please do not hesitate to ask us.

Sincerely,
Timco Koopman

Reviewer reports:

Gloria Pelizzo (Reviewer 1): This short report is a well written paper, suitable for publication in BMC pulmonary medicine. The report includes an important message: CPAM type 1, including thick walled multicystic air filled cysts larger than 2 cm in diameter, are strongly recommended for early surgery. The mucinous clusters, as premalignant precursors for mucinous adenocarcinoma, have to be excluded at histopathologic evaluation.

Reviewer 1 comment 1: Minor revision: B and C Ct scan figures could be presented under a better quality of images

Author response: we have replaced B and C in Fig1 (see file Fig1 Revised, uploaded separately) with higher quality images, acquired from the Radiology department’s system. We have included the radiologist in the Acknowledgements (line 167-168, page 8). However, the visual quality of the images has not improved much, as the original quality and resolution of the CT scans was limited due to the
small size of the patient; the girl weighed only 1.4 kilograms.

Csaba Galambos (Reviewer 2): This is an interesting report with new information regarding the oncogenic KRAS mutation present not only in the mucinous but also in the papillary component of CPAM 1.

Minor comments:

Reviewer 2 comment 1:
The molecular analysis needs to be more detailed. What method did authors use and and how did they make sure they analyzed the right areas?

Author response: we have provided a more detailed description of the molecular analysis (Case presentation, Molecular analysis, line 78-88, pages 4 and 5). We made sure we analyzed the right areas by annotating the areas for molecular analysis in the corresponding H&E slide; this has been added to the manuscript (Case presentation, Molecular analysis, line 76-78, page 4).

Reviewer 2 comment 2:
The author mentioned the presence of PIG, and I agree that PIG cells can be present in an expanded spectrum of developmental lung disorders. It is not clear however, what features the authors used to claim that the PIG is resolving, because it is well-known that PIG can be patchy. In addition, how did the authors exclude the possibility of sampling the PIG cells, and it is the PIG cells that carry the KRAS mutation?

Author response: The reviewer is right in commenting about the resolving aspect; the text has been adapted accordingly (Case presentation, Pathology, line 67-68, page 4. About excluding the PIG cells as source for the KRAS mutation: the PIG cells were present in the areas of the lung outside the CPAM area and within this CPAM area there were no recognizable PIG cells (as stated in Case presentation, Pathology, line 67: ‘glycogenosis in the alveolar septa in the non-involved part of the lobe’, see also the histology figures in Fig2). So we carefully selected primary epithelial areas with a surplus of epithelial cells and essentially no PIG cells, which corresponded with the 80% mutation rate in the molecular analysis.