Reviewer’s report

Title: Cascade Fumarate Hydratase mutation screening allows early detection of kidney tumour: a case report.

Version: 0 Date: 25 Nov 2016

Reviewer: Kiril Trpkov

Reviewer's report:

This case report is generally well written and may be a useful addition to the literature, provided it is adequately revised. The scenario is truly unique - a potential renal neoplasm discovered in a parent - due to FH def. Sy in the infant.

Major weakness of this manuscript is a very poor pathology description, which (likely) stems from the fact that no pathologist specialist in GU pathology was involved as a co-author. The topic of FH deficient - renal cell carcinoma (RCC) has undergone a major rethinking lately. Some of these data is quite novel and unsurprisingly the authors may not be aware of it. FH deficient RCC is NOT a papillary type 2 cancer (a concept which is challenged currently) - but it is a different type of extremely aggressive cancer (see Am J Surg Pathol 2016 Jul;40(7):865-75 and N Engl J Med. 2016;374:135-145). FH deficient RCC is also not restricted only to patients with frank HLRCC Sy. Also 'tubulocustic pattern' is frequently seen in FH-deficient RCC (Am J Surg Pathol. 2016 Nov;40(11):1457-1472). For screening purposes - IHC for FH and 2SC may be helpful. These and few other recent publications may be of interest and for inclusion in the revised discussion (for e.g. Am J Surg Pathol. 2014;38:627-637 and Am J Surg Pathol 2016;40(5):599-6070).

Major points:

1. The diagnosis of the renal lesion in the father as 'multilocular tubulocystic carcinoma' is questionable. Was this neoplasm tested for FH and 2SC by IHC? The lesion is not well illustrated at higher magnification and it may represent a 'cystic nephroma' - an incidental benign renal neoplasm. 'Tubulocustic pattern' is frequently seen in FH-deficient RCC (Am J Surg Pathol. 2016 Nov;40(11):1457-1472), but these are aggressive neoplasms. Provide additional IHC evidence for the diagnosis (or expert review) and provide better illustrations (higher mag. details and include prominent nucleoli in the neoplasm, if seen). This would be the key to make this case report credible! Also the quality of the photos is not good (the background should be white - not yellow!).

2. Papillary type 2 cancer is NOT what was thought to be associated with HLRCC and many experts now believe that papillary type 2 consists of multiple tumor types, recognized during
the last decade. Therefore, provide a statement that "type 2 papillary RCC" may not constitute a single entity, but may represent a pattern that may be seen in a variety of neoplasms, including, for example, Xp11 translocation RCC and collecting duct carcinoma, as acknowledged in the 2016 WHO Renal Tumor. Classification. This needs to be included in the discussion (replace sentences pertaining to Type 2 papillary RCC...lines 108-109, 114-115).

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.

Unable to assess

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

No

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

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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