Reviewer's report

Title: Whole exome sequencing reveals a stop-gain mutation of PKD2 in an autosomal dominant polycystic kidney disease family complicated with aortic dissection

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Reviewer: Federico Piscione

Reviewer's report:
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BMC Medical Genetics
Title: Whole exome sequencing reveals a stopgain mutation of PKD2 in an autosomal dominant polycystic kidney disease family complicated with aortic dissection

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a genetic hereditary systemic syndrome characterized by bilateral renal cysts, other potential cysts in several organs and extrarenal manifestations, including cardiovascular disorders. Case reports of aortic dissection (AD) in patients with ADPKD are currently limited and the underlying genetic aberration is rarely explored; of note, this article for the first time reports a case of ADPKD complicated with aortic dissection caused by PKD2 mutation, that is generally considered more "benign" compared to PKD1 mutation.

BMC Medical Genetics represents the appropriate journal for this study because it publishes papers which illustrate all aspects inherent genomics in relation to human health and disease.

Major Comments

1. Polycystins might be required to maintain vascular integrity but the precise mechanism by which specific PKD mutations predispose to a vascular phenotype remains unclear. Moreover, not all individuals from high-risk ADPKD families will experience vascular
complications. Can you explain the possible potential genetic mechanism of aneurysm formation of this stopgain mutation c.1774C>T, p.Arg592Ter detected in your case?

2. Despite congenital genetic aberration influence, hypertension represents the main risk factor for AD with a prevalence of about 75% in the overall AD. Can you better explain in the discussion the relationship hypertension-ADPK and the adding role of this classical cardiovascular risk factor in the development of dissection?

3. In the description of the case it's affirmed "He thereafter received blood pressure control therapy with multiple antihypertensive drugs"; can you better precise the therapy instaured? Are there in literature any drug associated with a slower decline of renal function and a low mortality rate in ADPKD patients?

4. The gene-mutation positive members of the family, even if asymptomatic, could benefit of an accurate screening program for cardiovascular complication; please underline in the discussion the importance to perform close clinical and echocardiographic screenings already at a young age in these subjects, suggesting the importance to introduce a molecular testing of ADPKD in similar situation. Moreover, what kind of instrumental examinations do you suggest for the follow-up of the patient of this case?

Minor Comments

1. All references must be numbered consecutively, in square brackets, in the order in which they are cited in the text and not listed in it with first author's name; please correct them.

2. The legend of figure 1 and 2 have been inverted; please change it in the correct order.

3. In the manuscript there are some grammar errors, particularly some sentences are too prolix. Please briefly review the language of entire article.

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.
I am able to assess the statistics

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