Author’s response to reviews

Title: A family pedigree of malignancies associated with BRCA1 pathogenic variants: A reflection of the state of art in China

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Reviewer reports:

Reviewer #1: Authors introduced most of the reviewers' comments, and the actual version of the manuscript is far better written.

However, there are some minor points, e.g.,

1) In the sentence on page 3 (line 49-52) the phrase "should accept" should be replaced with "should be offered".

Response: thank you! We have made the modification (page 3, line 50). The subtle change is a great respect to the autonomy of the patients. Great thanks to you!

2) The deletion of exon 8 BRCA1 have to be denoted according to nomenclature (http://varnomen.hgvs.org/)

Response: thank you! We have made the modification (page 4-5, line 83-84).

Nevertheless, my primary concern remains actual -the analysis of asymptomatic child is against general recommendations. And I am not fully- convinced with authors explanation. Did the author ask for the interpretation/permission local Review Board?

Response: thank you! We are touched by your enthusiasm on the protection of principles of nonmaleficence. We will follow your instructions in further clinical and research work. Here I dare to explain what happened in this child: After we revealed that deleterious variants in the adult family members, the child’s parents insisted on the testing for their child. We reported such
request to the administration director of our department and to the Institutional Review Board of Peking Union Medical College Hospital in oral and written memos. We had received official instructions from them that we must have detailed communication with their parents and get written consents from the child’s legal guardians before genetic testing. And we did. We just addressed your concern in the text, stating “after the permission from the Institutional Review Board of the study center” (page 5, line 96-97). However, we will rigorously follow the current recommendations and guidelines according to your instructions.

Reviewer #3: The manuscript has been improved. Please proceed to a proofreading before final submission.

Response: thank you! Great thanks for your help and instructions!

Please include the nomenclature of the BRCA1 PV. Refer to the LOVD database (https://databases.lovd.nl/shared/variants/BRCA1/unique).

Response: thank you! We have made the modification (page 4-5, line 83-84).