**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 #1: Overall this is a well-written case report highlighting significant limitations of BRCA1/2 testing in China. The authors report here a case of a four-generation family with BRCA1 pathogenic variant and aggregation of multiple malignancies. Additionally, they discuss in details the deficiencies in the national genetic-testing.

Main comments:

1) Please name mutation accordingly to the actual nomenclature

Response: Great thanks for your invaluable instructions! According to your instructions, we have modified the title (page 1, line 2-3) and the relevant text (page 5, line 83).

2) Analysis of other family members for the presence of a recognized variant is known as "co-segregation analysis" rather than "pedigree verification."

Response: Great thanks for your invaluable instructions! According to your instructions, we have modified the text. All the sayings of “pedigree verification” have been replaced by “co-segregation analysis” (page 3, line 29; page 4, line 51; page 6, line 86, line 89; page 8, line 129, line 137; page 11, line 204). Thanks!

3) The pedigree should be edited, instead of patients numbering include comments regarding the age of onset, type of cancer, etc.
Response: Great thanks for your invaluable instructions! According to your instructions, we have comprehensively modified the Figure 1. Great thanks!

4) The language should be polished.

Response: Great thanks for your invaluable instructions! We have sent the manuscript for another language editing, and a new certificate of language editing has been supplemented as an attachment.

5) Is the table 1 necessary? All that data can be presented on the pedigree

Response: Great thanks for your invaluable instructions! According to your instructions, we have deleted the Table 1, which is of course unnecessary.

However, my primary concern is the analysis of asymptomatic child, which is against general recommendations.

Response: Great thanks for your invaluable instructions! This is an extremely important problem. We have addressed your concern in the section of “Case presentation” (page 6, line 88-90) and in the section of “Discussion” (page 8, line 137-145). Despite extensive counseling and consent, the girl’s parents insisted on the test. In general, the potential impairment and injury of genetic testing on juveniles need further exploration. Rational counseling and informed consent should follow evidenced-based guidelines and the specific cultural environment, and should be driven by the best interest of the child. We have clarified this point in the text: “genetic testing for asymptomatic children in this report is beyond the authors’ consensus and general practice.”

Reviewer #2: This is an article of limited interest. There are discrepancies between the pedigree and the text (II-5 died or not?, where is II-7 in the pedigree?)

Response: Great thanks for your invaluable instructions! We are sorry for this stupid mistake. The patient of II-5 had died, and we have modified the figure 1. The II-7 is an incorrect reference of II-6, and we have modified the text (page 5, line 73) Terribly sorry for such mistakes! Wish you would forgive us!

The pedigree (Fig1) is of poor quality and should contain more informations (age, cancer, age of cancer,...)
Response: Great thanks for your invaluable instructions! According to your instructions, we have comprehensively modified the Figure 1. The error has been corrected, and the cancer patients’ information (age, type of cancer, age of onset of cancer) has been supplemented. Great thanks!