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# Comment on: Endometrial cancer occurrence five years after breast cancer in BRCA2 mutation patient

Min Chul Choi, Mi Sun Kim, Gee Hoon Lee, Jun Mo Lee

Comprehensive Gynecologic Cancer Center, Department of Obstetrics and Gynecology, CHA Bundang Medical Center, CHA University, Seongnam, Korea

We read with great interest the article by Oh et al. [1]. First of all, *BRCA2* mutation of the present case is unclassified variants (UVs). The results of the *BRCA1/2* genetic test is divided into mutations detected, not-detected and UVs mutations. UVs are referred to the ambiguous clinical significance and include: 1) missense mutations or small in-frame deletions whose effect on the protein structure cannot be immediately inferred; 2) variants, both exonic and intronic, that may potentially affect pre-mRNA splicing, but for which no direct evidence is available; and 3) variants in regulatory sequences. Their effect on cancer risk cannot be established through case-control association studies [2]. Clinical significance of UVs is listed as "unknown" in the Breast Cancer Information Core (BIC) database in most cases. The unclassified variants (c.1889C>T) of the present case is also listed as "unknown" in the BIC [3]. In order to clarify the meaning of this UV requires further studies, such as co-segregation test with family members or functional study. Therefore, it is hard to be determined the UV in the case as pathogenic mutation at this point.

In short, a female patient with family history of gastric cancer, which has affected by breast cancer and endometrial cancer sequentially, was discovered to have the *BRCA2* UV mutation after *BRCA* genetic test. It is hard to conclude that the breast and endometrial cancers caused by this UV mutation. Premature conclusion the UV as pathogenic or deleterious mutation may lead to a confusion to doctors, patient and patient's families. How will manage the unaffected carrier in the family of the present case and how will counsel these to the carriers?

Consider some aspects to present case. Whether other risk factors contributed to endometrial cancer of the patient, such as high body mass index (not mentioned in the article), breast cancer history and hormone therapy after mastectomy (letrozole not tamoxifen in the case). As mentioned earlier in the article, the lifetime risk of endometrial carcinoma is not associated with *BRCA* mutation [4]. The other point to consider is pathologically to review the specimen, especially the fallopian tubes and ovaries to discriminate synchronous malignancies.

Once the cause of confusion as above in this article is from what it might have been misunderstood the interpretation of the UV. I will introduce one case in our institution. A 42-year-old, early-staged, endometrioid cell type, ovarian cancer patient had *BRCA2* UV (8665_8667delGGA) at *BRCA* genetic test. This UV was found to be a pathogenic mutation after co-segregation test in her sister with breast cancer history. And her sister is now managed according to the NCCN guidelines considering as unaffected *BRCA* carrier. For patients and their families, it will be careful to draw pedigree, genetic counseling, genetic test and risks management.

## Conflict of interest

No potential conflict of interest relevant to this article was reported.

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Corresponding author: Min Chul Choi
Department of Obstetrics and Gynecology, CHA Bundang Medical Center, 59 Yatap-ro, Bundang-gu, Seongnam 463-712, Korea
Tel: +82-31-780-6191 Fax: +82-31-780-6194
E-mail: oursk79@cha.ac.kr

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