Genetic Characterization of Vietnamese Patients with Hereditary Breast and Ovarian Cancer Syndrome

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Introduction

Breast cancer is the most common cancer in Vietnamese women. Relative to the well characterized Caucasian population, little is known about predisposing genetic factors, especially in less-well characterized populations in Southeast Asia. As breast cancer is the leading cancer in women, it is important for public health to understand its causes in diverse populations. We report here the largest series of Vietnamese patients characterized for hereditary breast and ovarian cancer syndrome by advanced multi-gene sequencing technology.

Methods

We reviewed a series of 531 Asian patients evaluated between 2002 to 2018 with multi-gene testing. Of these, 24 were patients of Vietnamese ethnicity, with personal and/or family history of breast, ovarian, pancreatic and primary peritoneal cancer. All patients were female, with a mean age of 45 years, and underwent complete testing of coding exons *BRCA1/2*, *ATM*, *BRIP1*, *CHEK2*, *NBN*, *PALB2*, and *PTEN*, including flanking exon-intron junctions.

Patient	Age at Testing	Personal / Family History	Gene	Transcript	Variant	Pathogenicity	ClinVar
1	47	Half sister diagnosed with ovarian cancer	*BRCA1*	NM_007294.3	c.66dupA; p.Glu23ArgfsTer18	Pathogenic	Yes
2	31	Diagnosed with right ER+ PR+ HER2- breast cancer	*BRCA1*	NM_007294.3	c.1881_1884del; p.Ser628GlufsTer3	Pathogenic	Yes
3	64	Diagnosed with serous ovarian cancer	*BRCA1*	NM_007294.3	c.5251C>T; p.Arg1751Ter	Pathogenic	Yes
4	59	Diagnosed with breast cancer and transitional cell carcinoma of the ovary. Mother and sister diagnosed with breast cancer	*BRCA1*	NM_007294.3	c.5251C>T; p.Arg1751Ter	Pathogenic	Yes
5	53	Unknown	*BRCA2*	NM_000059.3	c.7052C>G; p.Ala2351Gly	VUS	Yes
6	36	Diagnosed with triple negative breast cancer	*BRCA2*	NM_000059.3	c.7052C>G; p.Ala2351Gly	VUS	Yes
7	62	Diagnosed with primary peritoneal cancer	*BRCA2*	NM_000059.3	c.3197A>G; p.Asn1066Ser	VUS	Yes
8	28	Diagnosed with ER+ PR+ HER2+ breast cancer. Paternal aunt diagnosed with breast cancer	*CHEK2*	NM_007194.3	c.665T>A ; p.Met222Lys	VUS	No
9	58	Diagnosed with serous ovarian cancer. Father diagnosed with lung cancer	*ATM*	NM_000051.3	c.79G>A; p.Val27Ile	VUS	No

Table 1. Summary of variants detected in 9 Vietnamese breast and/or ovarian cancer patients

Results

Pathogenic *BRCA1* mutations were detected in 4 of 24 patients (16.7%). *BRCA2* variants of uncertain significance (VUS) were also detected in 3 patients (12.5%). Importantly, all *BRCA1/2* variants detected were also reported in ClinVar, but the *CHEK2* and *ATM* VUSs detected are novel and have not previously been reported in ClinVar.

Discussion

This is the first multi-gene study in Vietnamese patients for hereditary breast-ovarian cancer syndrome. The prevalence of pathogenic *BRCA* mutations observed (16.7%) is considered very high in comparison to usual threshold recommendations in the West of 5-10% for testing. The cause of this is multifactorial, but highlights the importance of genetic factors for breast cancer among Vietnamese women. The observation that several variants have not been previously reported in international variant databases such as ClinVar highlight the need to better understand Vietnamese breast cancer genetics.

Conclusion

In the largest reported series of advanced multi-gene testing in Vietnamese women, we report a high percentage of pathogenic *BRCA* mutations, implying the importance of genetic testing for breast cancer in Vietnam. Additionally, a meaningful number of unreported genetic variants highlight the significance of recognizing ethnicity and evaluating less studied populations. These observations underline the need for greater investigation of the Vietnamese population for breast cancer disposition. Ongoing deeper studies of the Vietnamese population will allow for better breast cancer risk profiling and prevention.