Women who inherit BRCA gene mutations develop cancer earlier than their ancestors

September 12 2011

Women with a deleterious gene mutation are diagnosed with breast cancer almost eight years earlier than relatives of the previous generation who also had the disease and/or ovarian cancer, according to new research from The University of Texas MD Anderson Cancer Center.

The findings, published online in Cancer and updated since first presented at the 2009 Breast Cancer Symposium, could have an impact on how women at highest risk for the disease are counseled and even screened in the future, explained Jennifer Litton, M.D., assistant professor in MD Anderson's Department of Breast Medical Oncology.

"In our practice, we've noticed that women with a known deleterious BRCA gene mutation are being diagnosed earlier with the disease than their moms or aunts," said Litton, the study's first author. "With this study, we looked at women who had been both treated and had their BRCA testing at MD Anderson to determine if what we were seeing anecdotally was consistent scientifically, a phenomenon known as anticipation."

It's estimated that five to 10 percent of all breast cancers are associated with either the BRCA1 or 2 mutation, both of which are associated with an increased risk for breast and ovarian cancers. According to the American Cancer Society (ACS), women with BRCA1 or 2 have a 60 percent lifetime risk of developing breast cancer, compared to a 12 percent risk for women in the general population.

Given their greater risk, women with known BRCA mutations and/or whose mothers and/or aunts from either side of the family have the mutation are screened beginning at age 25. In 2007, as a complement to mammography, ACS guidelines added Magnetic Resonance Imaging (MRI) in the surveillance of these women at highest risk, as MRI is thought to catch smaller tumors even earlier. Consideration of prophylactic mastectomies is also a component of their surveillance, said Litton.

"Currently, BRCA positive women are counseled to start screening by 25 years, or five to ten years earlier than their youngest affected family member. However, our findings show that we may need to continue to follow these trends with future generations, and make changes accordingly in order to best advise and care for women at greatest risk," Litton said.

For the retrospective study, the researchers identified 132 BRCA positive women with breast cancer who participated in a high-risk protocol through MD Anderson's Clinical Cancer Genetics Program between 2003 and 2009. Reviewing each woman's pedigree (family tree), 106 were found to have a female family member in the previous generation who also had a BRCA-related cancer, either breast or ovarian. Age at diagnosis, location of mutation and birth year were recorded in both the older (gen1) and younger (gen2) women.

The study found that in gen2, the median age of diagnosis was 42, compared to age 48 in gen1. In comparing generations within a family, the median difference was six years. By using new mathematical models to evaluate for anticipation, the difference in age between generations was 7.9 years.

"These findings are certainly concerning and could have implications on the screening and genetic counseling of these women," Litton said. "In

BRCA positive women with breast cancer, we actually might be seeing true anticipation -- the phenotype or cancer coming out earlier per generation. This suggests more than the mutation could be involved, perhaps lifestyle and environmental factors are also coming into play."

The research reconfirms that women with BRCA mutations should continue to be screened per the guidelines - mammography, MRI and consideration of prophylactic surgeries - yet perhaps with increased suspicion and even at an earlier age, said Litton, who notes that the addition of MRI screening may account for some of the change in diagnosis seen in the study.

Further analysis is needed given the relatively small number of women in the cohort and the possibility of recall bias, as the gen2 women were providing their family histories, Litton explained. As follow up study, Litton plans to look into biological basis for potential earlier diagnosis.

Provided by Wiley

Citation: Women who inherit BRCA gene mutations develop cancer earlier than their ancestors (2011, September 12) retrieved 5 May 2024 from https://medicalxpress.com/news/2011-09-women-inherit-brca-gene-mutations.html