Rare cancer-causing syndrome found, for the first time, in Singapore

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A rare hereditary disorder that strongly predisposes carriers to develop cancer at an early age has been found in an Asian female, report researchers today at the American Association for Cancer Research Centennial Conference on Translational Cancer Medicine.

Generally, a person should have two normal copies of the powerful p53 tumor suppressor gene. But in the disorder known as Li-Fraumeni syndrome (LFS), one defective copy of p53 is inherited from a parent. Only about 400 families worldwide are known to have LFS, but none had been found in Singapore before this study, say researchers from the National Cancer Centre Singapore.

Although LFS is rare, it was found in a woman who had developed early onset breast cancer. Therefore, clinicians should also consider LFS as a potential diagnosis in young women with breast cancer, say the study investigators, Ann S.G.Lee, D.Phil., of the Division of Medical Sciences, Humphrey Oei Institute of Cancer Research, National Cancer Centre Singapore, and Peter Ang, M.Med., of the Department of Medical Oncology, National Cancer Centre Singapore.

“In a selected population of young breast cancer women with a family history suggestive of LFS, genetic testing may help to identify the syndrome,” said Lee. “Since LFS greatly increases the risk of developing several types of cancer, it would be important if it could be identified early. This would help persons at risk decide on certain health surveillances and other measures that might improve their long term health.”

People with LFS are at increased risk for developing multiple primary tumors of many different origins. In cancer patients who do not have LFS, cancer normally “knocks out” the normal function of p53 in order to grow and metastasize. But when a person only has one working copy of the gene to begin with, the chance that cancer will develop increases significantly, Lee says.

The prevalence of LFS in Singapore is unknown. Because one of the research interests of the National Cancer Centre Singapore is breast cancer susceptibility, investigators there decided to look for evidence of the syndrome in women who developed breast cancer at 35 years of age or younger. About four percent of breast cancer in Singapore is found in younger women, researchers say.

They recruited 30 patients and their families, took detailed family histories and tested their blood for mutations in the p53 gene and the CHEK2 gene, another tumor suppressor gene found to be mutated in some patients with LFS.

They found LFS in one woman in Singapore who had been diagnosed with breast cancer at age 25. Her mother had been diagnosed with breast cancer at age 34, and died at age 35, and a sister died of a brain tumor when she was 10 years old. The patient’s non-identical twin sister, determined by DNA fingerprinting, does not have LFS and does not have the p53 mutation found in her affected twin.

The researchers add that establishing a detailed family history that extends back for three generations, which is necessary to make a diagnosis of LFS, can be problematic. “In Singapore, many families are small and many are migrants, and it can be difficult to obtain the needed history,” Lee said. “That is why we focused our study on young onset breast cancer patients and tested these individuals for germ-line mutations in the p53 gene.”

Source: American Association for Cancer Research