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My46 Trait Profile

Li-Fraumeni syndrome

Other Names: SBLA syndrome (Sarcoma, Breast, Leukemia and Adrenal Gland)

Li-Fraumeni syndrome is a rare genetic condition where individuals have an increased chance of developing many different types of cancer. It is caused by mutations in the TP53 gene which makes a protein called tumor protein p53.

Characteristics of Li-Fraumeni syndrome

Li-Fraumeni syndrome (LFS) is a genetic condition that increases the risk of developing many types of cancer. There are two forms of LFS: the classic form of LFS and Li-Fraumeni-like (LFL) syndrome. LFL syndrome shares only some of the features of LFS. LFS is associated with an increased risk for different cancers including pre- menopausal breast cancer, lung cancer, bone and soft tissue sarcomas, leukemia, lymphoma, brain tumors, and adrenocortical cancer. Other cancer risks include ovarian, colon, skin, prostate, endometrial, stomach, and thyroid cancer. The risk of developing cancer by the age of 30 years is 50% and by the age of 80 years is 73-100%. Individuals with LFS also have an increased risk to develop multiple cancers. The overall risk to develop a second cancer is about 57% and the chance to develop a third cancer is 38%.

The incidence of these cancers in individuals with LFS varies depending on age. Sarcomas, adrenocortical carcinomas, and brain tumors (especially choroid plexus tumors) are most common before age 10. Bone sarcomas are frequently seen in the teenage years, and breast cancer and other brain tumors are seen after the age of 20.

Diagnosis/Testing

LFS can be diagnosed either by meeting certain clinical criteria or by genetic testing for a change or mutation in the TP53 gene. This gene makes a protein called tumor protein p53 that plays an important role in controlling cell growth. Mutations in TP53 gene allow for uncontrolled cell growth leading to the cancers associated with LFS. This is the only gene known to cause LFS. More than 70% of patients with a clinical diagnosis of LFS are found to have a mutation in this gene.

Management/Surveillance

Because of the wide range of cancers seen in LFS, there is currently no standard screening or surveillance protocol. However, management of LFS often involvesregular physical exams (for both children and adults) and increased screening for breast cancer (breast self exam, clinical breast exam, mammogram and breast MRI) and colon cancer (colonoscopy). Prophylactic mastectomy (i.e., preventive surgical procedure to remove a breast) is an option for women with LFS. Individuals with LFS should also have screening for specific organs based on the pattern of cancer that is seen in their families (targeted surveillance). In addition, all individuals should be evaluated by a physician if they have any symptoms or illnesses that are ongoing.

Mode of inheritance

LFS is inherited in an autosomal dominant pattern. This means inheriting one TP53 gene mutation is enough for an individual to be affected and show signs of LFS. The mutation can be inherited from an affected parent or it can be due to a new (de novo) mutation in an affected child.

Risk to family members

Individuals with LFS have a 50% chance of having a child with LFS. The risk to other family members depends on whether or not the individual with LFS has a parent affected with LFS. If a parent also has LFS, the risk for a sibling to have LFS is 50%. If a parent does not have LFS, the risk of other siblings being affected is low.

Special considerations

Individuals with LFS should avoid radiation therapy if possible. Radiation therapy can cause a second cancer diagnosis in individuals with LFS. As a result, women with LFS who have breast cancer might choose to have a mastectomy (i.e. surgical removal of an entire breast) instead of a lumpectomy (i.e., surgical removal of a lump in the breast) followed by radiation therapy. All individuals with LFS should avoid known carcinogens (e.g. cigarettes).

Resources

Li-Fraumeni Syndrome Association
http://www.lfsassociation.org/
Genetics Home Reference: Li-Fraumeni syndrome
http://ghr.nlm.nih.gov/condition/li-fraumeni-syndrome
Li-Fraumeni Syndrome Support Group
http://www.mdjunction.com/li-fraumeni-syndrome
Cancer.Net
http://www.cancer.net/cancer-types/li-fraumeni-syndrome

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