Li-Fraumeni Syndrome

Subjects: Genetics & Heredity
Contributor: Camila Xu

Li-Fraumeni syndrome is a rare disorder that greatly increases the risk of developing several types of cancer, particularly in children and young adults.

Keywords: genetic conditions

1. Introduction

The cancers most often associated with Li-Fraumeni syndrome include breast cancer, a form of bone cancer called osteosarcoma, and cancers of soft tissues (such as muscle) called soft tissue sarcomas. Other cancers commonly seen in this syndrome include brain tumors, cancers of blood-forming tissues (leukemias), and a cancer called adrenocortical carcinoma that affects the outer layer of the adrenal glands (small hormone-producing glands on top of each kidney). Several other types of cancer also occur more frequently in people with Li-Fraumeni syndrome.

A very similar condition called Li-Fraumeni-like syndrome shares many of the features of classic Li-Fraumeni syndrome. Both conditions significantly increase the chances of developing multiple cancers beginning in childhood; however, the pattern of specific cancers seen in affected family members is different.

2. Frequency

Li-Fraumeni syndrome is thought to occur in 1 in 5,000 to 1 in 20,000 people worldwide.

3. Causes

Li-Fraumeni syndrome is associated with mutations in the *TP53* gene. Nearly three-quarters of families with Li-Fraumeni syndrome and about one-quarter with Li-Fraumeni-like syndrome have germline mutations in the *TP53* gene. Germline mutations are typically inherited and are present in essentially every cell in the body. *TP53* is a tumor suppressor gene, which means that it normally helps control the growth and division of cells. Mutations in this gene can allow cells to divide in an uncontrolled way and form tumors. Other genetic and environmental factors are also likely to affect the risk of cancer in people with *TP53* mutations.

A few families with cancers characteristic of Li-Fraumeni syndrome and Li-Fraumeni-like syndrome do not have *TP53* mutations. The genetic factors involved in these cases are unclear.

3.1. The gene associated with Li-Fraumeni syndrome

- TP53

4. Inheritance

Li-Fraumeni syndrome is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to increase the risk of developing cancer. Most people with Li-Fraumeni syndrome inherit an altered copy of the gene from an affected parent. In 7 to 20 percent of cases, however, the altered gene is the result of a new (de novo) mutation in the gene that occurred during the formation of reproductive cells (eggs or sperm) or very early in development.

For a cancer to develop in Li-Fraumeni syndrome, a mutation involving the other copy of the *TP53* gene must occur in the body's cells during a person's lifetime. Cells with two altered copies of this gene do not make functional TP53 protein, which allows tumors to develop. Almost everyone who inherits one *TP53* gene mutation will eventually acquire a mutation in the second copy of the gene in some cells. The second mutation often occurs in cells within the breast, bone, or muscle tissue, typically leading to the tumors common in Li-Fraumeni syndrome.

5. Other Names for This Condition

- LFS
- sarcoma family syndrome of Li and Fraumeni
- sarcoma, breast, leukemia, and adrenal gland (SBLA) syndrome
- SBLA syndrome

References

1. Batalini F, Peacock EG, Stobie L, Robertson A, Garber J, Weitzel JN, Tung NM. Li-Fraumeni syndrome: not a straightforward diagnosis anymore-the interpretation of pathogenic variants of low allele frequency and the differences betweengermline PVs, mosaicism, and clonal hematopoiesis. Breast Cancer Res. 2019 Sep18;21(1):107. doi: 10.1186/s13058-019-1193-1. Review.
2. Chompret A. The Li-Fraumeni syndrome. Biochimie. 2002 Jan;84(1):75-82.
3. Gargallo P, Yáñez Y, Segura V, Juan A, Torres B, Balaguer J, Oltra S, CastelV, Cañete A. Li-Fraumeni syndrome heterogeneity. Clin Transl Oncol. 2020Jul;22(7):978-988. doi: 10.1007/s12094-019-02236-2.
4. Kratz CP, Achatz MI, Brugières L, Frebourg T, Garber JE, Greer MC, HansfordJR, Janeway KA, Kohlmann WK, McGeeR, Mullighan CG, Onel K, Pajtler KW, PfisterSM, Savage SA, Schiffman JD, Schneider KA, Strong LC, Evans DGR, Wasserman JD,Villani A, Malkin D. Cancer Screening Recommendations for Individuals withLi-Fraumeni Syndrome. Clin Cancer Res. 2017 Jun 1;23(11):e38-e45. doi:10.1158/1078-0432.CCR-17-0408. Review.
5. Melean G, Sestini R, Ammannati F, Papi L. Genetic insights into familialtumors of the nervous system. Am J Med Genet C Semin Med Genet. 2004 Aug15;129C(1):74-84. Review.
6. Moule RN, Jhavar SG, Eeles RA. Genotype phenotype correlation in Li-Fraumenisyndrome kindreds and its implications for management. Fam Cancer.2006;5(2):129-33. Review.
7. Olivier M, Goldgar DE, Sodha N, Ohgaki H, Kleihues P, Hainaut P, Eeles RA.Li-Fraumeni and related syndromes: correlation between tumor type, familystructure, and TP53 genotype. Cancer Res. 2003 Oct 15;63(20):6643-50.
8. Strong LC. General keynote: hereditary cancer: lessons from Li-Fraumenisyndrome. Gynecol Oncol. 2003 Jan;88(1 Pt2):S4-7; discussion S11-3. Review.
9. Varley JM. Germline TP53 mutations and Li-Fraumeni syndrome. Hum Mutat. 2003Mar;21(3):313-20. Review. Erratum in: Hum Mutat. 2003 May;21(5):551.
10. Wong P, Verselis SJ, Garber JE, Schneider K, DiGianni L, Stockwell DH, Li FP, Syngal S. Prevalence of early onset colorectal cancer in 397 patients withclassic Li-Fraumeni syndrome. Gastroenterology. 2006 Jan;130(1):73-9.