Li-Fraumeni Syndrome and the Role of the Pediatric Nurse Practitioner

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Li-Fraumeni syndrome (LFS) is an inherited cancer syndrome that affects a small percentage of the population worldwide. LFS is characterized by multiple cancers in affected family members and is devastating to all diagnosed patients and their relatives. A link has been identified between LFS and mutations in the tumor-suppressor gene that encodes for the P53 protein, and much research has been done on the effect of this mutation in tumorigenesis. However, the natural history of the disease has no definitive pathway, and additional research is under way. LFS is rare, can present in many ways, requires complex management, and has tumors that often first present in childhood. Therefore, pediatric nurse practitioners should be aware of LFS as a potential differential diagnosis in patients with multiple tumors, certain rare tumors, or most importantly, a family history notable for multiple early-onset cancers.

L i-Fraumeni syndrome (LFS) is a rare genetic cancer syndrome characterized by a predisposition of affected family members to a broad spectrum of cancers. In 1969, Li and Fraumeni described four families with multiple cases of cancer. Li and Fraumeni (1969) defined LFS as the diagnosis of a sarcoma in an individual by age 45 with at least two first-degree relatives with any type of cancer that was diagnosed before age 45. LFS is an autosomal dominant disorder linked with germline mutations in the tumor-suppressor gene *TP53* (Malkin et al., 1990). *TP53* is one of the most frequently altered identifiable genes in cancer; it encodes the P53 protein, which plays a role in antiproliferation of various target genes (Moule, Jhavar, & Eeles, 2006) (see Figure 1). Therefore, germline mutation in *TP53* increases the risk for multiple types of cancers; patients with LFS have up to a 90% lifetime risk for developing cancer (Royds & Iacopetta, 2006). Figure 2 lists a glossary of terms.

The definition of LFS has been argued over time; both classic LFS and Li-Fraumeni–like syndromes are described in the literature. Classic LFS retains the definition originally described by Li and Fraumeni (1969), although the types of cancers associated with true LFS have grown to include any soft tissue sarcoma, osteosarcoma, breast cancer, brain tumors, leukemia, and adrenocortical carcinoma (Li et al., 1988). Li-Fraumeni–like syndromes are broken down further into syndromes with certain

At a Glance

✦ Li-Fraumeni syndrome (LFS) predisposes patients and their families to multiple types of cancer throughout their lives.

✦ LFS is a clinical diagnosis based on familial cancers but has been linked to mutations in the tumor-suppressor gene *TP53*.

✦ As genetics continues to play a role in healthcare management, nurses and nurse practitioners should maintain a current knowledge base to provide optimal patient care.

diagnostic criteria that are less restrictive than those for LFS. In classic LFS, *TP53* germline mutations are found in at least 70% of cases (Izawa et al., 2008); however, not all individuals with LFS are tested for mutations. *TP53* mutations tend to be found less frequently in Li-Fraumeni–like syndromes; however, the cancer risk of those affected still is increased greatly (Olivier et al., 2003).

Although rare (Oppenheim, Brugieres, Chompret, & Hartmann, 2001), LFS is devastating to those affected. Most individuals with LFS have an onset of cancer as children or adolescents; as a result, specific ethical issues are associated with genetic testing, screening, and management, particularly in the