DURING AND AFTER TREATMENT

Germline (Hereditary) Risk

Mary L. Schmitt, MS, FNP-BC, APRN, AOCNP®

For germline (hereditary) risk, standards of care are based on emerging evidence-based practice.

Definition

- Cancer may affect any individual, but some people are at higher risk than others. The majority of cancer cases are sporadic, caused by DNA damage that may occur in one cell (not an egg or sperm) and accumulate over a lifetime.
- Hereditary predisposition to cancer is caused by pathogenic variants in certain genes passed from parent to offspring through the egg or sperm and referred to as germline. In hereditary cancer syndromes, higher incidence, earlier age at onset, and patterns of cancer may be seen within families.
- Most hereditary cancer syndromes are passed from parent to offspring in an autosomal dominant pattern.
- In autosomal dominant inheritance, a genetic condition occurs when a pathogenic variant is present in only one allele (copy) of a given gene.
  - ☐ With each conception, a child has a 50% chance of inheriting a pathogenic variant.
- Some hereditary cancer syndromes follow an autosomal recessive pattern of inheritance.
  - ☐ If both parents are carriers of the same pathogenic variant and both pass it to the child, the child will be affected. Those with one copy of the pathogenic variant are carriers and may or may not have an increased risk for developing cancer.
- Penetrance is the proportion of people with a particular pathogenic variant who exhibit signs and symptoms of a genetic disorder. Penetrance for hereditary cancer is considered incomplete and may occur in a greater percentage of individuals (high-penetrance genes) or moderate or low percentages (moderate- or low-penetrance genes) (National Cancer Institute [NCI], n.d.; Tung et al., 2016).

Incidence

- About 5%–10% of all cancers are associated with hereditary cancer syndromes, most of which are inherited in an autosomal dominant manner. Hereditary cancer testing is recommended for individuals with a personal or family history that indicates an increased risk of cancer or known pathogenic variant in the family (National Comprehensive Cancer Network [NCCN], 2021a, 2022).

Pathophysiology

- An inherited pathogenic variant in one copy of a tumor suppressor gene and subsequent acquired pathogenic alteration in the second copy leads to the two-hit model of tumor development, in which the loss of heterozygosity and increased genomic instability lead to the development of carcinogenesis (Syngal et al., 2015).

Hereditary Risk Factors

- Younger than age 50 years with a cancer diagnosis
- Personal history of more than one cancer diagnosis
- More than 20 adenomatous polyps or serrated polyps
- Rare cancers (e.g., ovarian, pancreatic, medullary thyroid cancer, pheochromocytoma, paraganglioma)
- Microsatellite instability on colon or endometrial cancer tumor
- High allele count on tumor testing in a gene associated with germline risk
- Family members with the following:
  - ☐ Male breast cancer
  - ☐ Ovarian cancer
  - ☐ Multiple family members with breast, colon, or endometrial cancer (particularly when younger than age 50 years)
  - ☐ Known genetic pathogenic variant
  - ☐ Pancreatic cancer
  - ☐ More than 20 adenomatous polyps (NCCN, 2021a, 2022)

Baseline Assessment

- Hereditary cancer risk assessment begins with a personal and thorough family history that covers at least three generations

PROVIDER RESOURCES

GeneReviews®
- www.ncbi.nlm.nih.gov/books/NBK1116

MedlinePlus
- https://medlineplus.gov/genetics/understanding

National Comprehensive Cancer Network (NCCN)

NCCN Guidelines®: Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic [v.1.2022]
- www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf

NCCN Guidelines®: Genetic/Familial High-Risk Assessment: Colorectal [v.1.2021]
- www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf