Changes in the 2011 NCCN Hereditary Breast and Ovarian Cancer Guidelines

Genetics and Your Practice

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Very recently, the National Comprehensive Cancer Network (NCCN) updated their guidelines for genetic/familial high-risk assessment for breast and ovarian cancer. I’d like to take this opportunity to briefly review some of the changes to the guidelines that affect whom to refer for genetic testing, and how to manage affected patients. In this article, I will focus on the changes to the hereditary breast and ovarian cancer syndrome guidelines, although there were also some minor changes to the Li-Fraumeni and Cowden syndrome guidelines, respectively.

There is an important change to the HBOC testing criteria. The previous criteria (v 1.2010) included:

- Individuals from a family with a known BRCA1/BRCA2 mutation
- Personal history of breast cancer plus one or more of the following:
  - Diagnosed at ≤45 y
  - Diagnosed at age ≤50 y with ≥1 close blood relative with breast cancer ≤50 y and/or ≥1 close blood relative with epithelial ovarian/fallopian tube primary peritoneal cancer at any age
  - Two breast primaries when first breast cancer diagnosis occurred prior to age 50
  - Diagnosed at any age, with ≥2 close blood relatives with breast and/or epithelial ovarian/fallopian tube/primary peritoneal cancer at any age
  - Close male blood relative with breast cancer
  - Personal history of epithelial ovarian/fallopian tube/primary peritoneal cancer
  - For an individual of ethnicity associated with higher mutation frequency (Ashkenazi Jewish) no additional family history may be required
- Personal history of epithelial ovarian/fallopian tube/primary peritoneal cancer
- Personal history of male breast cancer
- Family history only -- first, second or third degree relatives (3rd must have ≥2 close blood relatives with breast cancer ≤50 y and/or ovarian at any age) meeting any of the above criteria.

The revised criteria for HBOC testing have added important new points for affected individuals and a slight clarification to the recommendation for individuals with family history only:

- Affected: Triple negative (ER-, PR-, HER2-) breast cancer diagnosed <60 y
- Affected: Diagnosed age < 50 y with a limited family history (see clarification below)
- Affected: Personal history of breast and/or ovarian cancer at any age with ≥2 close blood relatives with pancreatic cancer at any age
- Affected: Personal history of pancreatic adenocarcinoma at any age with ≥2 close blood relatives with breast and/or ovarian and/or pancreatic cancer at any age
- Family history only: Third-blood relative with breast cancer and/or ovarian/fallopian tube/primary peritoneal cancer with ≥2 close blood relatives with breast cancer (at least one with breast cancer ≤50 y) and/or ovarian cancer

The guidelines point out that individuals with limited family history, such as fewer than two first or second degree female relatives or fewer than two female relatives surviving beyond 45 years may have an underestimated risk for a mutation. Importantly, the guidelines also point out that patients who have received an allogeneic bone marrow transplant should not have molecular genetic testing via blood or buccal samples due to the contamination by donor DNA. In those cases, DNA should be extracted from a fibroblast culture.

The new pancreatic cancer additions to the guidelines point to the importance of recognizing pancreatic cancer risk related to BRCA2 mutations. We also published a review of PALB2-related data that links breast and pancreatic cancer in rare families last month in this newsletter, which also reiterates the importance of referring families with significant history of breast and pancreatic cancers. The guidelines also clarified examples of other BRCA founder mutation populations (outside of Ashkenazi Jewish) include Icelandic, Swedish, Hungarian and Dutch. Finally, a footnote was added regarding genetic testing for BRCA mutations in children under age 18 y is generally not recommended. This, of course, is family history dependent, and in rare cases adolescents may be tested.

In addition to the changes for risk assessment and testing for HBOC, there are also some minor changes to the guidelines for management of HBOC. Previously, “regular monthly breast self exam (BSE) starting at age 18 y” was formally recommended, but it has now been removed for affected women and men. Another important clarification regards the possibility of short-term hormone replacement therapy (HRT) that is recommended for discussion when counseling women who undergo risk-reducing salpingo-oophorectomy (RRSO) before natural menopause. It now reads “…possible short term HRT to a recommended maximum age of natural menopause…”. Previously, the timing of short-term HRT was not identified in the recommendations. Finally, timing of CA-125 screening for women who do not elect RRSO was changed to “after day 5 of menstrual cycle in premenopausal women” and breast MRI is recommended to be performed day 7-15 in the menstrual cycle (instead of 1-15 as previously published).

Genetic counseling by an appropriately trained professional is advised when genetic testing is offered and often after results are disclosed per current NCCN guidelines. If you have a patient that you’d like to refer for genetic risk assessment, please contact your friendly genetic counselor at 817-838-4871.

Reference: