Genetics of Hereditary Breast and Ovarian Cancer

The majority of cancer cases are not attributable to hereditary causes. However, cancer can be hereditary in some families. Many factors can increase the probability that the cancers in a family may be hereditary. Some of these factors are: early onset of cancer (e.g. premenopausal breast cancer), more than one primary (new) cancer in an individual, the same cancer in two or more close relatives on the same side of the family, unusual presentation of cancer (e.g. breast cancer in a male) and related cancers (such as breast/ovarian/pancreatic cancer) found in the same family. Individuals of Ashkenazi Jewish ancestry are also at greater risk for hereditary breast and ovarian cancer. In addition, emerging data suggest that certain features are overrepresented in hereditary breast and ovarian cancer syndrome, including medullary and ‘triple negative’ tumors (estrogen receptor (ER) negative, progesterone receptor (PR) negative and HER2 negative or ‘ER-/PR-/HER2-’).

Several gene changes (mutations) have been discovered which predispose individuals to breast and ovarian cancer. In review, the genetic instructions for our bodies are stored in our cells in tiny structures called chromosomes. A typical individual has 23 pairs of chromosomes: one chromosome from each pair is inherited from the mother, and the other from the father.

Two genes account for a majority of hereditary breast and ovarian cancer cases. These are BRCA1 (breast cancer-1, located on chromosome #17) and BRCA2 (breast cancer-2, located on chromosome #13).

Both of these genes are passed down in families in a pattern called autosomal dominant. This means that a parent who carries the gene has a 50% chance of passing the gene on to each of their children. It also means that if a person carries such a mutation, their siblings have a 50% chance to carry the mutation.

Genetic testing for mutations in BRCA1 and BRCA2 has become clinically available within the past fifteen years. The available data suggests that women who carry mutations in the BRCA genes have between a 50-85% risk to develop breast cancer and as great as a 15-60% risk to develop ovarian cancer (this includes cancer of the fallopian tubes) by the time they are 70 years of age. These figures are significantly higher than the 12-13% lifetime risk for breast cancer and the 1-2% lifetime risk for ovarian cancer in the general population. Carriers also have a greater chance of developing additional primary breast cancers in remaining breast tissue (as high as ~20-60% lifetime risk). Males who carry mutations in either BRCA gene have a slightly increased lifetime risk to develop prostate cancer and males who carry BRCA2 mutations are at increased risk to develop male breast cancer (~5-10% lifetime risk). Individuals with BRCA2 mutations have an increased risk for pancreatic cancer (~4-8% lifetime risk) and perhaps melanoma.

Individuals who learn they have a BRCA1 or BRCA2 mutation are offered special surveillance and risk reduction options. Genetic testing for BRCA1 and BRAC2 is available at age 18 as there are no known childhood cancers for mutation carriers. High-risk screening typically begins at age 25 for women and age ~35 for men.