Genetic testing for BRCA1 and BRCA2 genes

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Mrs. R is a healthy 53-year-old female. She is married with two daughters and is of Ashkenazi Jewish descent. She sees her nurse practitioner (NP) for her annual exam and screenings. During the visit, she asks the NP about genetic testing for breast cancer. She recently read about genetic testing and has done some research online. She is concerned because her mother was diagnosed with breast cancer at age 32 and is deceased. Additionally, her maternal grandmother died from ovarian cancer at age 50.

The NP explains to Mrs. R that based on her family history and her Ashkenazi Jewish descent, she is a candidate for BRCA1 and BRCA2 genetic testing. The NP further explains that knowing if there is a mutation helps Mrs. R and her healthcare providers to stratify her risk of developing breast or ovarian cancer. The decision to undergo genetic testing rests with the patient, but it is important for NPs to provide all the options for screening and management available so an informed decision can be made.

The NP also explains that there are federal laws in place that protect her genetic information and privacy and that her test results will only be shared with healthcare providers involved in her circle of care. The Genetic Information Nondiscrimination Act established significant protections against genetic discrimination by employers and health insurers. This act prohibits health insurance carriers from denying coverage because an individual took or refused to take a genetic test or from denying coverage based on test results. It also prohibits employers from using this information as the basis for employment decisions.1

It is important for patients to be aware that, at this time, there are no special protections against the use of genetic information to inform the provision of life insurance, disability insurance, or long-term care.

The purpose of the article is to describe genetic testing for breast cancer. Genetic testing for many diseases is becoming more readily available. NPs must understand how to utilize these tests and interpret results for their patients in the primary care setting.

BRCA1 and BRCA2
Breast cancer susceptibility gene 1 (BRCA1) and breast cancer susceptibility gene 2 (BRCA2) belong to a group of genes identified as tumor suppressors.2 In normal cells, these tumor suppressors establish stability of the cell’s genetic information by helping repair DNA and making proteins that help regulate cell growth.2,3 Gene mutations in BRCA1 and BRCA2 have been associated with the development of hereditary breast cancer.2 Several of these mutations alter one of the amino acids used to create BRCA1 protein, resulting in a protein that cannot perform its usual DNA function of repair.2 As these mutations congregate, they can allow cells to divide and grow rapidly, resulting in the formation of a tumor.3

Mutations in this gene may also increase the risk of other types of cancer including ovarian, fallopian tube cancer, pancreatic cancer, and male breast cancer.3 The gene can be inherited from either parent, mother, or father. A BRCA mutation occurs in 5% to 10% of all breast cancers and about 15% of overall ovarian cancers.4

Genetic testing
Information from genetic testing provides a way to identify patients who have an increased risk of developing disease.5 Genetic information can come from biological samples of DNA, family history of disease, physical exam findings, and medical records.5 Family history may serve as the first step in identifying patients with an inherited cancer predisposition that produces an especially high lifetime risk of cancer.5 A predictive gene test is used to look for gene mutations that might place a person at risk for getting a disease, such as cancer.6 DNA is taken from the patient’s blood or saliva to test for the BRCA gene mutations, and the sample is sent out for analysis.7

Mutation is a change in the usual DNA sequence of a particular gene that can have damaging effects on health.5 DNA-based testing may be used to determine whether the individual has inherited a disease-related mutation.8 Results from genetic testing by healthcare providers can only be disclosed by the healthcare provider and labs in limited circumstances permitted by state and privacy laws including Health Insurance Portability and Accountability Act.7
Genetic counseling

Prior to receiving genetic testing, a genetic counselor may be able to help the patient understand what to anticipate, the advantages and disadvantages of the testing, how the results may affect the patient and her family, management options, and how to incorporate the results into their daily life. The counseling process can involve only the patient and her family, and may require several visits to address all of the issues.

The purpose of genetic counseling is to supply the patient with unbiased information regarding the test so she is prepared to make an informed decision about whether or not to have the test completed. There are occasions in which testing is essential, and the patient’s practitioner will recommend the testing and follow up. The patient has a right to refuse the test in any situation.

A positive test

A positive test result generally indicates that the woman has inherited a known BRCA1 or BRCA2 mutation, consequently, increasing the risk of developing breast cancer. This result only provides information about a woman’s risk of developing breast cancer. The positive result cannot say whether or not that woman will actually develop breast cancer or when. Not all women will develop breast cancer if they inherit a harmful BRCA1 or BRCA2 mutation.

There are several options available for patients who have inherited a harmful BRCA1 or BRCA2 mutation. Surveillance methods, or breast cancer screenings, are ways of detecting the disease early via mammography, clinical breast exams, and magnetic resonance imaging (MRI). Using these methods may help to identify the cancer in its early and most treatable stage.

Prophylactic mastectomy is an option that will remove the healthy tissue from the bilateral breasts in order to decrease the chance of developing breast cancer. This surgery does not guarantee that the patient will not develop breast cancer, but it decreases the chance.

Chemoprevention is the use of synthetic or natural substances or medications to reduce the risk of developing breast cancer or to decrease the chance of returning cancer. Evaluating each patient’s medical situation and risk must be cautiously reviewed to make sure the harmful effects of the medications do not outweigh the benefits.

Some patients consider changing certain lifestyle behaviors as an option that can affect their risk of developing cancer. These behaviors may include limiting alcohol consumption, increasing physical activity, and eating a low-fat diet. It is unclear how effective lifestyle modifications are at reducing cancer risk for those with known genetic mutations.

The value of a negative test

Patients who test negative, yet carry a family history for an elevated risk for breast or ovarian cancer, meet criteria for more intense surveillance than a patient at average risk. A woman with a first degree relative affected is about twice as likely to develop breast cancer. In addition, the risk in developing breast cancer is higher when the relative was diagnosed under age 50 and when there are numerous affected relatives.

If the patient’s test result comes back negative for the BRCA gene, it is important to know her risk. Tyer-Cuzick model, Gail model, and the Claus model are available for practitioners to help estimate the risk a woman has for developing breast cancer. Risk management includes an annual mammogram and a clinical breast exam every 6 to 12 months for patients with a strong family history of breast and ovarian cancer who test negative for BRCA1 and BRCA2. An annual MRI, as an adjunct to mammogram and clinical breast exam, may be recommended for women with at least a 20% lifetime risk of breast cancer.

Pros and cons of BRCA1 and 2 genetic testing

There are advantages and disadvantages to genetic testing. The possible advantages of having a test with a negative result include a sense of relief from uncertainty and the possibility that special preventive tests, checkups, or surgeries may not be necessary. In a similar way, having a positive test result can help patients to make informed decisions about their future and what steps can be taken to reduce their risks of breast cancer.

Genetic testing can potentially cause psychological, emotional, and financial distress for individuals, their family, and their social relationships. Genetic tests do not give defined answers about the inherited disease. A positive result does not guarantee that the individual will develop breast cancer, nor does a negative result guarantee that breast cancer will not develop. The tests suggest what might happen, not what will happen.

Creating a support system

Mrs. R’s test results return positive for the BRCA1 deleterious mutation. An appointment has been scheduled with her NP to discuss her results. She is referred to Gynecology to discuss ovarian cancer screening, with preference toward a bilateral oophorectomy, since she has completed childbearing. She is also referred to a breast surgeon to discuss options for breast surveillance or prophylactic mastectomies with reconstruction.
An appointment is scheduled with oncology to discuss chemoprevention and any further management that may be needed.

It is of utmost importance for the NP to enable Mrs. R to create a support system to guide and support her in the decision-making process. She is advised to share her test results with appropriate family members, especially her daughters, as they each have an increased risk of inheriting the gene mutation.

Lastly, she is referred to various support groups in her community and nationally, as these organizations can provide support and information during the difficult decision-making process. Confronting hereditary cancer is a complicated, highly individualized journey, and support is critical.

REFERENCES

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