Understanding Hereditary Breast and Ovarian Cancer

Karen A. Roesser, RN, MS, AOCN®

In 1994, the first cancer susceptibility gene to be associated with hereditary breast and ovarian cancer was identified and became known as breast cancer gene 1 (BRCA1). In 1995, a second gene was identified and became known as BRCA2 (Culus, Schildkraut, Thompson, & Rissh, 1996). With the identification of these two genes, a new field emerged in breast and ovarian cancer treatment that is transforming how a select population of people with these cancers is managed. However, the identification of these cancer susceptibility genes also has prompted new challenges and concerns, including identifying patients who are appropriate for genetic testing, informing patients about the advantages and disadvantages of genetic testing, and determining the appropriate treatment for those who test positive for a genetic mutation (alteration). In addition, ethical, legal, and psychosocial implications for patients and their families exist.

As knowledge of cancer genetics has increased, so has awareness of cancer genetics among healthcare professionals and the public. Oncology nurses can be instrumental in informing patients, families, and the public about the implications of these findings in terms of cancer prevention, early detection, and treatment. In addition, knowledge in this area has become essential to healthcare professionals when obtaining family histories to help identify patients who may have hereditary cancers.

Recognizing the importance of this area in oncology nursing, the Oncology Nursing Society (ONS) has developed position statements regarding cancer predisposition genetic testing and risk assessment counseling and the role of oncology nurses in cancer genetic counseling. ONS stated that oncology nurses at the general and advanced practice levels must be educated in genetic testing and counseling and continuing education programs should be developed and provided to practicing oncology nurses. In addition, advanced practice nurses with specialized training in cancer genetics should provide comprehensive cancer genetic counseling (ONS, 2002a, 2002b).

Case Study

R.J. is a 32-year-old woman who was referred to a surgeon because of a palpable lump in her right breast. Her mammogram also identified this 2 cm x 2 cm mass. R.J. had an excisional biopsy that revealed a fibroadenoma. The surgeon noted that R.J. had a positive family history of breast cancer in her mother and a maternal aunt. A maternal cousin also had ovarian cancer. R.J. was of Irish and English heritage. The surgeon referred her to a genetic counselor for possible hereditary breast and ovarian cancer testing. After extensive counseling, R.J. consented to undergo testing. The findings were positive for a deleterious mutation (a change that results in an altered or damaged protein, rendering it unable to perform its function) in BRCA1.

1. What percentage of patients with breast cancer is thought to have a hereditary predisposition for breast or ovarian cancer?
   a. Less than 2%
   b. Approximately 5%
   c. Approximately 13%
   d. More than 50%

2. What factor in R.J.’s history does not suggest an increased risk for hereditary breast or ovarian cancer?
   a. History of breast cancer in her aunt
   b. History of breast cancer in her mother
   c. Diagnosis of fibroadenoma
   d. History of ovarian cancer in her cousin

3. Which option currently is not being used as a possible medical intervention for women with a BRCA1 mutation?
   a. Surveillance measures for breast and ovarian cancer
   b. Bilateral prophylactic mastectomy and oophorectomy
   c. Radiation therapy to the breast and abdomen
   d. Chemopreventive measures for breast and ovarian cancer

Discussion

Question 1: Choice b, approximately 5%, is correct. Although all cancer is genetic because it results from mutations in genes that normally control cell division, most mutations are acquired during patients’ lifetimes. However, in a small subset of people, mutations may be inherited. Researchers estimate that, in 2003, more than 200,000 women will develop breast cancer. Of these women, approximately 5% are thought to have a hereditary basis for the development of the disease (American Cancer Society, 2003).

Hereditary breast and ovarian cancer are associated with mutations in BRCA1 or BRCA2. Genes are pieces of DNA that are found on chromosomes and are the functional unit of heredity that express inherited traits (see Figure 1). Each gene

Karen A. Roesser, RN, MS, AOCN®, is an oncology clinical nurse specialist in the Thomas Jefferson Cancer Center at the Chippenham Johnston Willis Medical Center in Richmond, VA.

Key Words: breast neoplasms; ovarian neoplasms; Brca1 gene, Brca2 gene; genetic counseling; neoplasms, hereditary

Digital Object Identifier: 10.1188/03.CJON.591-594
contains instructions for making a protein that does the work of the cell. Thus, abnormalities in the genes (i.e., mutations) result in changes in the protein that may prevent it from working correctly.

The majority (84%) of hereditary breast cancer results from inherited mutations in BRCA1 and BRCA2 (Ford et al., 1998). BRCA1 and BRCA2 are tumor-suppressor genes. The proteins encoded by tumor-suppressor genes normally prevent cells from becoming malignant. The risk of cancer increases only when mutations in these genes prevent the proteins from working properly. Women with a BRCA1 or BRCA2 mutation are believed to have a lifetime risk of 56%–87% for developing breast cancer (Ford et al.). This is considerably higher than the usual risk factors associated with an increased risk for breast cancer, which include early menarche, older than age 30 at the birth of a first child, history of breast cancer in the family, and use of postmenopausal hormone replacement therapy.

**Question 2: Choice c, diagnosis of fibroadenoma, is correct.** The diagnosis of a fibroadenoma has not been associated with an increased risk of developing hereditary breast or ovarian cancer. Choice a, history of breast cancer in her aunt; choice b, history of breast cancer in her mother; and choice d, history of ovarian cancer in her cousin, are factors that may increase R.J.’s risk for breast or ovarian cancer. Based on R.J.’s family history, she should be referred to an advanced practice nurse with specialized training in cancer genetics or a genetic counselor.

Healthcare professionals should obtain detailed family histories of patients who may be at increased risk for the development of hereditary breast and ovarian cancer. At least three generations should be reviewed with a focus on first- and second-degree relatives on both sides of the family. After this information is documented, it should be arranged in a standard pedigree format (Barse, 2003). Figure 2 shows a pedigree of R.J.’s genetic family history.

Hallmarks of possible hereditary breast and ovarian cancer that are related to R.J.’s history include early age of breast cancer onset (before age 50), multiple affected family members, transmission across generations, and the presence of ovarian cancer. If two or more individuals in the same family are affected with the same cancer (or, in this case, breast or ovarian cancer), the cause may be a hereditary cancer syndrome, particularly if those affected with breast cancer are younger than age 50. In addition, in hereditary breast cancer, paired (bilateral) organs often are involved (Armstrong, Eisen, & Weber, 2000).

Although R.J.’s genetic mutation appears to be transmitted on the maternal side of the family, an autosomal dominant pattern of transmission of BRCA1 or BRCA2 exists, meaning that the likelihood that this mutation could be passed on by her mother or father is the same. Therefore, each offspring of a BRCA mutation carrier has a 50% likelihood of acquiring the genetic mutation.

Information regarding patients’ ethnicity may be important to assess because certain mutations occur in some cancer-predisposing genes (BRCA1 and BRCA2) and are specific to certain ethnic groups. Although these muta-
tions have not been significant in people of Irish and English heritage, the occurrence has been significant in the Ashkenazi (eastern and central European) Jewish population. Mutations specific to this population result from a phenomena called the “founder effect,” which occurs when a population is descended from a relatively small number of people (“founders”) without a substantial influx of people outside the group. As a result, a limited number of different chromosomes are distributed widely among the population (Abeliovich et al., 1997).

Several models have been established to predict patients’ risk of developing a particular cancer or estimate patients’ chances of carrying a mutation in particular cancer-susceptibility genes. The latter risk is important for those who are considering genetic testing. Risk models that have been used to determine mutation prevalence of BRCA1 or BRCA2 include Couch, Shattuck-Eidens, and BRCAPRO models. Different models and methods are appropriate for different purposes. The Couch Model estimates the chance of carrying a BRCA1 mutation and is based on families with an average of 3.5 cases of breast or ovarian cancer (Couch et al., 1997). The Shattuck-Eidens Model also calculates the possibility of carrying a BRCA1 mutation and reviews risk factors associated with BRCA1-carrier status including early-onset breast cancer, bilateral breast cancer, ovarian cancer, and Ashkenazi Jewish heritage (Shattuck-Eidens et al., 1997). The mathematical BRCAPRO calculates the probability that women with family histories of breast or ovarian cancer carry a BRCA1 or BRCA2 mutation. This model considers family history including first- and second-degree relatives and age at diagnosis and death of affected family members (Berry, Parmigiani, Sanchez, Schildkraut, & Winer, 1997). In reviewing R.J.’s family history, a genetic counselor determined R.J.’s risk of having a deleterious BRCA1 or BRCA2 mutation.

Table 1 was used to compute that risk by considering patient and family history of breast and ovarian cancer and age of disease onset. Based on this table, R.J. had a risk of 16.7% that she would be found positive for such a mutation. The American Society of Clinical Oncology (1996) stated that a discussion about the possibility of genetic testing should occur with patients whose risk for a BRCA1 or BRCA2 mutation is 10% or greater. Those guidelines currently are under revision with many experts offering testing on an individual basis after reviewing patients’ personal and family histories.

After assessing family history, developing a pedigree, and determining patients’ risk for carrying a mutation in BRCA1 or BRCA2, communicating genetic-testing options to patients in a well-balanced and supportive environment is important. The primary focus should be helping patients understand their potential genetic risk, the risks and benefits of genetic testing, and the issues related to genetic information. Cancer surveillance and risk reduction options, implications for other family members, and ethical, emotional, and psychosocial issues related to genetic information need to be conveyed to patients. The risks of genetic testing include the potential for a breach in confidentiality of the genetic information, for insurers to deny medical coverage if a cancer risk exists, and for anxiety and emotional suffering if the test is positive. Patients should make an informed decision to undergo or forego testing based on comprehensive information and support provided by healthcare providers.

**Question 3:** Choice c, radiation therapy to the chest and abdomen, is correct. The use of radiation therapy to the chest and abdomen would not be an option at this time. Radiation therapy has not been used prophylactically to treat breast or ovarian tissue in women who have a deleterious mutation in BRCA1.

Choice a, surveillance measures for breast and ovarian cancer, should be part of the overall management plan. The option of close surveillance for breast and ovarian cancer would be discussed. Breast cancer surveillance includes yearly or semiannual mammograms beginning immediately, monthly breast self-examinations, and semiannual mammograms beginning immediately, yearly breast self-examinations, and semiannual mammograms beginning immediately.

**Table 1. Prevalence of Deleterious Mutations in BRCA1 and BRCA2 (Excludes Individuals With Ashkenazi Ancestry)**

<table>
<thead>
<tr>
<th>Patient's History</th>
<th>No Breast Cancer (BC) Before Age 50 or Ovarian Cancer (OC) in Any Relative (BC) (%)</th>
<th>BC Diagnosis Before Age 50 in One Relative and No OC in Any Relative (BC) (%)</th>
<th>BC Diagnosis Before Age 50 in More Than One Relative and No OC in Any Relative (BC) (%)</th>
<th>OC at Any Age Before Age 50 in Any Relative (%)</th>
<th>OC in More Than One Relative and No BC Before Age 50 in Any Relative (%)</th>
<th>BC Diagnosis Before Age 50 and OC at Any Age (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No BC or OC at any age</td>
<td>2.9</td>
<td>4.2</td>
<td>9.8</td>
<td>5.8</td>
<td>8.7</td>
<td>16.7</td>
</tr>
<tr>
<td>BC at or after age 50</td>
<td>3.2</td>
<td>8.3</td>
<td>11.4</td>
<td>7.4</td>
<td>9.8</td>
<td>19.8</td>
</tr>
<tr>
<td>BC before age 50</td>
<td>7.8</td>
<td>17.8</td>
<td>31.6</td>
<td>16.7</td>
<td>31.2</td>
<td>44.5</td>
</tr>
<tr>
<td>Male BC</td>
<td>20.4</td>
<td>23.8</td>
<td>50.0*</td>
<td>–</td>
<td>NT</td>
<td>100.0*</td>
</tr>
<tr>
<td>OC at any age and no BC</td>
<td>11.9</td>
<td>29.3</td>
<td>38.8</td>
<td>24.7</td>
<td>32.2</td>
<td>51.4</td>
</tr>
<tr>
<td>BC at or after age 50 and OC at any age</td>
<td>17.6</td>
<td>21.1*</td>
<td>43.8*</td>
<td>18.2*</td>
<td>44.4*</td>
<td>50.0*</td>
</tr>
<tr>
<td>BC before age 50 and OC at any age</td>
<td>32.0</td>
<td>56.7</td>
<td>72.2*</td>
<td>58.8*</td>
<td>62.5*</td>
<td>81.3</td>
</tr>
</tbody>
</table>


**N = 10,231**

**NT—none tested**

* N < 20

**Includes family members with either or both diagnoses**
breast examinations performed by a healthcare professional. Surveillance for ovarian cancer also would be addressed. Although thought to be much less effective than breast cancer screening, the options discussed would be yearly or semiannual transvaginal ultrasound, pelvic examinations, and testing for the cancer antigen CA-125 (Burke et al., 1997).

Choice b, bilateral prophylactic mastectomy and oophorectomy, is incorrect because these potential medical interventions could be used. However, the inherited mutation is present in all body cells, so cancer still can develop after a prophylactic procedure. All prophylactic surgical options should be discussed with patients, including a surgical bilateral mastectomy. The removal of all breast tissue would reduce the occurrence of breast cancer by at least 90% (Hartmann et al., 2000). In addition, prophylactic oophorectomy also should be considered. Oophorectomy not only can reduce the risk of ovarian cancer by more than 95%, but it also can reduce the risk of breast cancer in women with BRCA mutations by nearly 50% (Rebeck, 2002). In a woman of age 30, such as R.J., this option would be discussed. However, because she is not past childbearing age, she may decide to defer this option until a later date or when childbearing is completed.

Choice d, chemopreventive measures for breast and ovarian cancers, should be discussed with patients. The risk of breast cancer can be reduced by using selective estrogen receptor modulators such as tamoxifen. Tamoxifen has been found to decrease the risk of breast cancer by 45% in women who are at increased risk for the development of the disease. At this time, the effectiveness of tamoxifen in risk reduction related to those who are positive for BRCA1 mutations is not known. Women who carry BRCA1 mutations tend to develop estrogen-receptor–negative tumors (King et al., 2001).

The role of oral contraceptives to reduce the risk of ovarian cancer should be addressed. Although the use of oral contraceptives for six years or more is associated with a 60% reduction in the hereditary risk of ovarian cancer (Narod et al., 1998), their use in hereditary breast and ovarian cancer remains controversial.

Conclusion

With the discovery of BRCA1 and BRCA2, a new area of cancer genetics has emerged. Determining appropriate candidates for genetic testing and discussing the risk-to-benefit ratio of testing are essential. Taking a thorough and accurate family history is a necessary first step in assessing both sides of the family, because half of all BRCA1 or BRCA2 mutations are inherited from the paternal side of the family. Those elements of a family history that suggest the need for further evaluation are breast cancer diagnosis before age 50, male breast cancer, ovarian cancer at any age, breast and ovarian cancer in the same person, Ashkenazi Jewish ancestry, and relatives known to carry a mutation in BRCA1 or BRCA2. Genetic testing should be performed only in the setting of pre- and post-test counseling and only after obtaining patients’ fully informed consent. Patients who test positive for a genetic mutation in BRCA1 or BRCA2 will be counseled on the options of increased surveillance, chemoprevention, and prophylactic surgery.

Author Contact: Karen A. Roesser, RN, MS, AOCN®, can be reached at karen.roesser@hcahealthcare.com.

References


