Case 5: Impact of hereditary breast and ovarian cancer genes on male family members

Rob, the son of Janet (see Case 1), is 32. He and his wife have a 4-year-old daughter and are planning to have additional children soon. After learning about her mother-in-law's diagnosis, his wife asks their family doctor if Rob should undergo genetic testing. Rob's wife would like to know if he has a mutation before becoming pregnant again. She has heard about preimplantation genetic diagnosis and would like to know more about their options for avoiding passing on a mutation to their child. Rob is reluctant to pursue testing; he feels healthy and does not see the benefit of testing.

Questions

Which family members should consider genetic testing first?

The best person to undergo genetic testing in a family with a medical history suggestive of hereditary breast and ovarian cancer (HBOC).) is the family member(s) most likely to carry a mutation. This is usually a family member with a cancer diagnosis suggestive of HBOC, such as those with ovarian cancer, young-onset breast cancer, or triple-negative breast cancer. However testing an affected family member is not always possible, especially when those affected by cancer have already passed away.

What is cascade testing?

Cascade testing is the favored approach for testing relatives in a family with an identified mutations that causes hereditary breast and ovarian cancer (HBOC), in which first degree relatives of the proband with the mutation are tested and then additional peoples are tested that are related to each family member who is found to carry the mutation. Cascade testing is a cost-effective approach to testing because the cost is low and the pre-test probability of identifying a mutation carrier is high.

Should men in families with inherited risk of ovarian and breast cancer consider testing? Is there special surveillance recommended for men?

Men with *BRCA1* and *BRCA2* mutations have an increased cancer risk that is higher than an average man's risk but not as high as the risk for women with *BRCA1* and *BRCA2* mutations. This risk is higher for men with *BRCA2* mutations than *BRCA1* mutations. The cancers associated with mutations include:

- Male breast cancer
- Prostate cancer
- Pancreatic cancer
- Melanoma

NCCN guidelines for risk-management in men with mutations include:

- Breast self-exam training and education starting at age 35 years
- Clinical breast exam, every 12 months, starting at age 35 years
- Starting at age 40 years:
    - Recommend prostate cancer screening for *BRCA2* mutation carriers
    - Consider prostate cancer screening for *BRCA1* mutation carriers

The above recommendations constitute a change from usual medical care and provide justification for testing men for BRCA1 and BRCA2 mutations. However, insurance companies do not always pay for testing in men.

What is the role of preimplantation genetic testing in families with *BRCA1* and *BRCA2* mutations?

Preimplantation genetic diagnosis (PGD) can be used to select and implant embryos that do not have a mutation. PGD would require that Rob's wife also undergo in vitro fertilization (IVF). These procedures can be costly and are often not covered by health insurance. Financial assistance programs are available to offset costs. In general, PGD is utilized more commonly for genetic diseases in which outcomes are severe or affected offspring are at risk for disease in childhood, especially if no prevention methods are available, while the risk with *BRCA1* and *BRCA2* mutations is for cancer as an adult, with significant potential for screening and risk reduction.