The Angelina Jolie Story and The Issue of Gene Testing

As a result of the Angelina Jolie story women are now asking many more questions about the potential benefits of gene (BRCA1/2) testing. Angelina watched her mother die of ovarian cancer, and she also had a maternal aunt who had breast cancer. Because of her family history she was tested for the BRCA gene and was found to be positive (i.e. she inherited a mutated BRCA from her mother and inherited a normal BRCA gene from her father). As a result of this inherited mutation she had an approximate 80% lifetime risk of developing breast cancer. She made a personal decision to have both breasts removed (bilateral prophylactic mastectomies). Her surgery reduced her lifetime risk of developing breast cancer to approximately 5% which is lower than that for the average women whose lifetime risk is approximately 12%.

The Angeline Jolie story is important because it brings to light the issues of genetic testing and risk reduction. Hopefully, her story will motivate women with family histories of breast or ovarian cancers to participate in risk assessment programs.

The actual number of women in the general population who have the BRCA mutation is only one in 400. However, there is a much larger number of high risk women who test negative for the BRCA gene, but would also benefit from more aggressive breast cancer screening. In this issue of “Ask the doctor” I will attempt to clarify the issue of which women would benefit from genetic testing and also identify those women who are not gene positive but who would also benefit from more aggressive breast cancer screening.

“Am I at increased risk for developing breast cancer” is a question that every woman should ask. Because of the evolving complexity of determining who is at risk, it is helpful to divide risk into three levels. At low risk are those women with no family history of breast or ovarian cancer and who have fatty breasts on their mammograms. For these women, a monthly Breast Self Exam (BSE), yearly mammogram, and yearly physician exam is all that is recommended. Women in this low risk group have a less than 12% lifetime risk of developing breast cancer.

At the other end of the spectrum are the high risk women like Angelina Jolie who had a family history of both breast and ovarian cancer. Other “red flag” issues that are indicators of the need for gene testing are having a family member who develops a breast cancer before the age of 50 or a family member who has been diagnosed with cancers in both breasts. Also, women should be concerned if multiple family members have had breast cancer. Another important risk factor is a male family member with breast cancer. Finally, women of Ashkenazi descent should consider gene testing if there is any family history of breast cancer (see end of this article for a more detailed outline of who should be tested for a BRCA mutation).

The issue of who should be tested can be very challenging as is illustrated in a case that was seen in our high-risk clinic. We recently treated a 39 year old woman who was diagnosed with breast cancer who stated that she had no family history of breast or ovarian cancer. Because of her young age, a BRCA test was performed and she tested positive (we routinely do genetic testing for the BRCA gene in women who develop breast cancer and are 45 years of age or younger). After a long investigation, it was determined that both her father and grandfather carried the gene, but it was not expressed (i.e. they did not have breast cancer) as is commonly the case in males who carry the gene. As a result of testing positive for the gene, she elected to have both breasts removed rather than the originally planned lumpectomy. This case illustrates the complexity of identifying women at risk, and serves as a reminder that some women will carry the mutation without obvious risk factors.

The issue of breast density has also added confusion to the issue of risk assessment. As we discussed in last

month's issue of Ask the Doc, breast density is also a risk factor for developing breast cancer. All women with dense breasts should consider having supplemental breast imaging (see last month's Ask The Doctor article). In an attempt to summarize the issue of risk assessment and gene testing I suggest the following:

Low risk women:
No family history and fatty breasts on mammograms: No additional imaging or gene testing indicted
High risk women:
Strong family history of breast or ovarian cancer (see list at end of article): Gene testing and yearly MRI
Women in the middle (majority of women):
Dense breasts and a family history of breast cancer:
- Consider a risk assessment consultation
- Consider a yearly screening ultrasound (or yearly MRI if very concerned)

Dense breasts and no family history:
- Consider a yearly screening ultrasound

Fatty breasts and a family member with breast cancer:
- Consider the option of a risk assessment consultation.
- No additional imaging required in most cases.

I hope this basic outline is helpful. If you have questions, Ask The Doctor or Contact Us. Next month I will answer the 7 basic questions that are commonly asked about BRCA testing.

Who should be tested for a BRCA mutation?

General guidelines for BRCA testing:
The likelihood of a harmful mutation in BRCA1 or BRCA2 is increased with certain familial patterns of cancer. These patterns include the following:

For women who are not of Ashkenazi Jewish descent:
- two first-degree relatives (mother, daughter, or sister) diagnosed with breast cancer, one of whom was diagnosed at age 50 or younger;
- three or more first-degree or second-degree (grandmother or aunt) relatives diagnosed with breast cancer regardless of their age at diagnosis;
- a combination of first- and second-degree relatives diagnosed with breast cancer and ovarian cancer (one cancer type per person);
- a first-degree relative with cancer diagnosed in both breasts (bilateral breast cancer);
- a combination of two or more first- or second-degree relatives diagnosed with ovarian cancer regardless of age at diagnosis;
- a first- or second-degree relative diagnosed with both breast and ovarian cancer regardless of age at diagnosis; and
- breast cancer diagnosed in a male relative.

Women of Ashkenazi Jewish descent:
- any first-degree relative diagnosed with breast or ovarian cancer; and
- two second-degree relatives on the same side of the family diagnosed with breast or ovarian cancer.