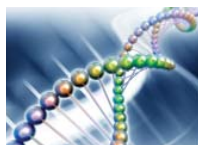


ERYNN GORDON, MS, CGC



What PAs should know before they refer patients to a genetic counselor

Medical genetics is an evolving field. Historically it encompassed only rare Mendelian disorders and chromosome abnormalities with multisystem phenotypes. Because of their medical complexity combined with the risk to other family members and the psychosocial issues that arise when dealing with issues of inheritance, these cases were best handled by geneticists and genetic counselors. Now, a growing number of diseases have been recognized as having a genetic basis, and relegating genetics just to the geneticists and genetic counselors has become more difficult. Moreover, identification of those aspects of genetics that can be incorporated into primary care has become more important. Key to this process is identifying when to refer a patient to a geneticist or a genetic counselor. Many factors come into play, as demonstrated by the following case:

CASE STUDY

A 50-year-old woman of Ashkenazi Jewish ancestry has been given a diagnosis of invasive breast cancer; her mother died of breast cancer at 48 years, and her sister's ovarian cancer was diagnosed at age 52. Based on that history, the woman was at risk of carrying a mutation in *BRCA1* or *BRCA2*, the two genes known to cause hereditary breast and ovarian cancer syndrome.

After meeting with a genetic counselor whose area of expertise was cancer, the patient learned more about what carrying a *BRCA1* or *BRCA2* mutation meant. If she had such a mutation, each of her three daughters

would be at a 50% risk to inherit it as well. Those who carry a *BRCA* mutation have a 65% to 85% lifetime risk of breast cancer^{1,2} and an 11% to 54% lifetime risk of ovarian cancer.^{1,2}

The counselor offered genetic testing to determine whether the patient carried a *BRCA* mutation. In addition to the implications for her daughters, a positive result would mean that the patient herself was at increased risk for developing a second breast cancer and/or ovarian cancer. Given the weight of this information, she and her husband decided that they needed to think about whether they were ready to know more and to share this information while they were in the midst of dealing with the current breast cancer diagnosis and treatment.

Several months later the couple decided, for their daughters' sake, to proceed with testing.

After blood was drawn, the patient made an appointment with the genetic counselor to receive the results in person. Two days before that appointment, the patient called to cancel, explaining that she could not handle the information at that time. Several follow-up calls and cancelled appointments later, she came in for her results. (Figure 1 shows her genetic pedigree.) Though not surprised that she tested positive for a *BRCA1* mutation, the patient was devastated by the implications this would have for her daughters. The genetic counselor offered to work with the patient to share this information with her daughters and

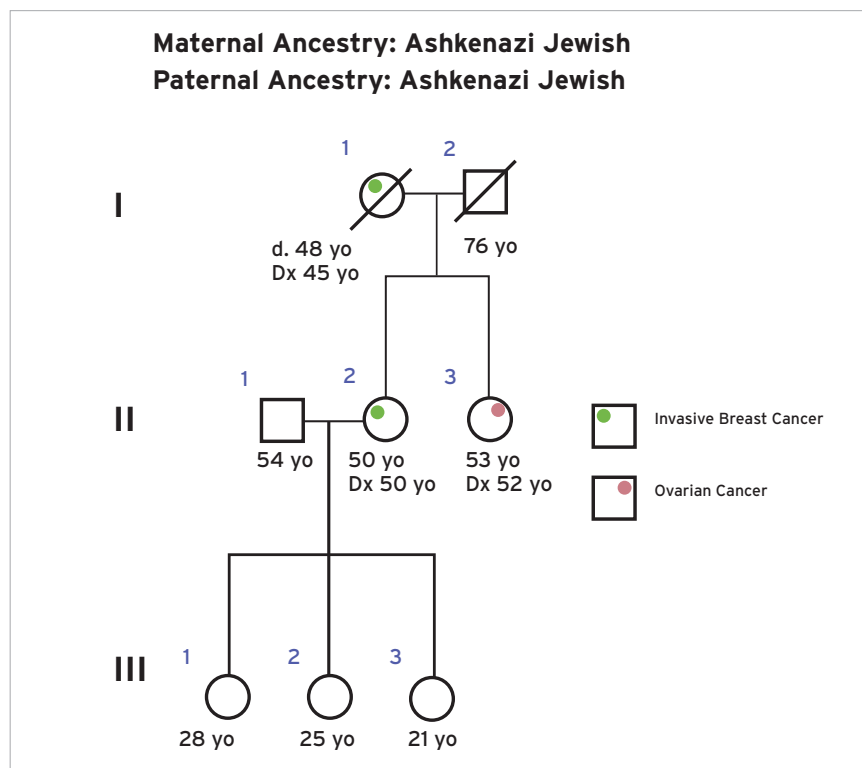


FIGURE 1. The patient's genetic pedigree

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referred her to FORCE: Facing Our Risk of Cancer Empowered, a support group for women at high risk for breast cancer and/or ovarian cancer.

Not every scenario involving genetic counseling is as emotionally charged as this one. Still, this patient's story illustrates the additional emotional burden and guilt often associated with hereditary conditions.

DISCUSSION

When to refer a patient to a genetic counselor can depend on many factors: a clinician's understanding of the disease, the resources accessible to the clinician, and the geographic accessibility of a geneticist or genetic counselor.

Access to a professional with the ability to appropriately interpret and communicate the results of tests and to

prospectively advise the patient on the implications (medical, psychosocial, and financial) is a particularly important consideration. Appropriate interpretation may seem like a no-brainer; after all, the laboratory provides an interpretation. However, many genes can cause the same disease, and a single genetic test may capture only a small percentage of cases, so negative

Follow-up to genetic assessment in determining disease risk

Erynn Gordon, MS, CGG; Michael Rackover, PA-C, MS

In an earlier article, "The role of genetic assessment in determining a patient's disease risk" ("Genomics in PA Practice," May 2009), we presented a patient's genetic pedigree and the results of his genetic testing and asked readers how they would counsel him. Even without the genetic test results, several findings in the patient's family history were noteworthy. First, the combination of pancreatic cancer and breast cancer in a family of Ashkenazi Jewish descent suggests the possibility of a *BRCA1* or *BRCA2* gene mutation. Although *BRCA1* and *BRCA2* are most often associated with an increased risk of breast and ovarian cancer, there is also an association with other cancers, including prostate cancer; melanoma; and pancreatic cancer, with one study finding *BRCA* mutations in 5.5% of Ashkenazi Jewish patients with pancreatic adenocarcinoma.¹ This finding, in combination with a higher rate of *BRCA1* and *BRCA2* mutations (three common mutations) in the Ashkenazi Jewish population, makes this history worth investigating further. In addition, the paternal family history of acute MI, pulmonary embolism, and deep venous thrombosis raises questions about a hereditary cardiovascular risk factor. However, given the variety of ages at onset, some of which were late in life, further investigation of other cardiovascular risk factors, such as weight, smoking status, and various comorbidities, is also warranted. Finally, one cannot ignore the fact that multiple family members were reported to be infertile. If desired, a fertility workup should be considered.

The additional information provided by genetic testing adds another dimension to this patient's risk assessment. While the family history of glaucoma alone is not concerning (one second-degree relative affected), testing showed that the patient is homozygous for the *LOXL1* gene, which raises his risk of glaucoma to 3.4% (triple the average population risk of 1.1%). The family history combined with the

genetic test result suggests that the patient is at increased risk for glaucoma and warrants a referral for glaucoma screening. Note, however, that based on the genetic factors alone, he has a 96.6% chance of *not* developing glaucoma and should be following screening schedules based on national recommendations issued by such organizations as the American Academy of Ophthalmology and the American Optometric Association.

Finally, we must consider the patient's doubled risk for prostate cancer based on his having six of eight genetic risk markers. This risk is significant, and referral to a urologist is appropriate. We must be careful to avoid putting undue emphasis on these risk factors, however, as the four genetic variants studied (we all have two copies of each gene, yielding eight potential risk markers) represent only a portion of the genetic risk for prostate cancer. Heritability studies show that 42% of the risk for prostate cancer is genetic (of which these eight genetic risk factors represent only a portion) and 58% of the risk is environmental.² Presently, the greatest known risks for prostate cancer are race (African-Americans are at highest risk) and family history.³ Bringing the patient's family history back into focus, recall that *BRCA2* founder mutations in the Ashkenazi Jewish population have also been associated with an increased risk of prostate cancer.⁴ Although mutations in *BRCA2* were not included in this patient's genetic testing, the results have brought the important issues of his family history and genetics to the forefront and could be the catalyst for additional testing.

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results may not rule out risk for the condition. An adequate understanding of the detection rate, what percentage of cases is captured by a genetic test, and what a positive or a negative result can mean (ie, whether the result rules out the diagnosis or does not rule out the diagnosis) is essential.

Medical practice often requires the clinician to convey life-altering information, such as a diagnosis of cancer or the identification of a birth defect on prenatal ultrasound. Hereditary conditions create unique circumstances, however, in which anticipatory guidance about the implications of the results is often needed. Sometimes patients learn about their risk of a genetic predisposition prior to experiencing any symptoms. They may learn about a risk to their children. Or they may learn about potential future medical complications (for example, the risk of aortic aneurysm in someone with Marfan syndrome). In such cases, the clinician's role is to ensure that patients understand the magni-

“The clinician’s role is to ensure that patients understand the magnitude of the information they would receive from genetic testing.”

tude of the information they would receive from genetic testing, that they actually want that information, and that they are prepared to deal with it, regardless of the treatment options (or lack thereof), all before the test is even ordered. We often worry most about people who want presymptomatic testing for devastating neurodegenerative conditions, such as Huntington’s disease, but there can be enormous psychological pressure associated with learning genetic test results after the patient is symptomatic, as illustrated by the case presented.

Ultimately, no concrete list of circumstances can guide a clinician to decide when to refer and no magical powers are possessed by geneticists and genetic counselors. The process is similar to

deciding to refer to any other specialist, and it can be guided by some simple questions: Are you equipped (with knowledge, resources, colleagues) to give this patient the best care as it relates to this situation? Are you prepared to discuss the implications of being tested? Will you subsequently be able to interpret the results? [JAAPA](#)

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