With Genetic Testing, Don't Forget Duty to Warn

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MIAMI BEACH — Obstetrician-gynecologists can identify patients and families at risk for genetic cancers, provide appropriate referrals, and monitor patients with long-term follow-up, Talia Donenberg, a board-certified genetic counselor, said at an ob.gyn. conference sponsored by the University of Miami.

And they can meet with patients to review and update the management plan, update family history, and provide support as needed, said Ms. Donenberg of the Center for Cancer Prevention and Genetics, University of Miami.

Ovarian cancer has one of the highest frequencies of inheritance, at least 10%, she said. "It is important to define patient-specific risk."

There are legal liability implications. "Now that we have commercially available genetic testing, it is important to discuss risk of other cancers for them and their family members," Ms. Donenberg said. There is the issue of duty to warn. "So far there have been three lawsuits against physicians about failure to warn patients about a family predisposition." In a recent case, a woman being treated for bilateral breast cancer claimed her physician never discussed her familial risk for ovarian cancer. The lawsuit was settled out of court.

Initial genetic counseling can take up to 2 hours at the multidisciplinary, high-risk screening clinic where Ms. Donenberg counsels and tests patients referred from primary care providers and specialists. One aim is to get at least a three-generation pedigree. "The accuracy of reporting breast cancer is higher than with ovarian cancer. When they report a family history, was it really ovarian cancer, or was it endometrial or cervical?"

Certain clues can help genetic counselors if a person's recollection is incomplete. For example, "it is inconsistent with ovarian cancer if a family member was diagnosed at age 30 and remained asymptomatic for another 30 years," Ms. Donenberg said. Unusually early onset of cancer (younger than 50), multiple primary tumors in the same patient, and bilateral breast cancer are other indicators of hereditary cancer, she said. "Also, unusual cancers, such as male breast cancer, might tip us off."

Begin genetic testing with an affected family member if possible, Ms. Donenberg said. "Often the proband is a woman who is unaffected but concerned."

The clinic receives grant funding for testing of indigent patients. "This is extremely important because genetic testing is very expensive," Ms. Donenberg said. It can cost more than $3,000 to look at both BRCA1 and BRCA2 genes. Most insurance companies will cover the testing if the right criteria are met, she added.

It costs considerably less—about $400—to test for a single mutation in an at-risk family member, Ms. Donenberg said.

In addition, it is less costly and easier to find a specific BRCA mutation in patients from certain populations with recurring founder mutations, such as Ashkenazi Jews.

Hereditary susceptibility to epithelial ovarian cancer for a BRCA1 carrier is 50%-60%, and for a BRCA2 carrier, the risk is 30%-40%, Ms. Donenberg said. Investigators have also calculated cumulative cancer risk by age in BRCA carriers (Science 2003;302:643-6).

BRCA-related ovarian cancer is often nonmucinous, poorly differentiated, and invasive. Borderline tumors are highly unlikely, Ms. Donenberg said. The mean age of onset is 52 years. Most of these cancers originate in the fallopian tubes.

BRCA-related ovarian cancer has been associated with a better response to chemotherapy and better overall prognosis (Cancer 2003;97:2187-95).

Management options for BRCA mutation carriers include prescription of oral contraceptives. Use of these agents for 5-6 years reduced breast cancer risk by 60% in one study (J. Natl. Cancer Inst. 2002;94:1773-9). Surveillance every 6 months starting at ages 25-35 is also suggested.

Prophylactic salpingo-oophorectomy is another option, Ms. Donenberg said. This surgery reduces risk of primary ovarian and fallopian cancers, "and we have data this can reduce breast cancer risk in premenopausal women (N. Engl. J. Med. 2002;346:1616-22).

"There is a large proportion of these women who already have occult ovarian cancer at time of a prophylactic procedure. This is something we have to keep in mind," Ms. Donenberg said. ■