Honing the Health Message on BRCA Mutations

By Charlie Schmidt

Angelina Jolie’s announcement that she had undergone a double mastectomy to ward off potential tumors induced by her BRCA1 mutation served as what Kenneth Offit, MD, called a teachable moment.

“Public figures can have seismic impacts on health communication when they speak about their own experiences,” said Offit, chief of the Clinical Genetics Service at the Memorial Sloan–Kettering Cancer Center (MSKCC) in New York. “Angelina Jolie’s disclosure was no exception.”

After the actress revealed her surgery with a May 17 editorial in the New York Times, Offit and other well-known cancer specialists appeared on news outlets around the country, coalescing around several core themes:

- BRCA mutations statistically significantly elevate risks for both breast cancer (according to Offit, from 40% to 87% for BRCA1 and from 30% to 80% for BRCA2) and for ovarian cancer (up to 50%).
- Only a tiny fraction of breast and ovarian cancers can be attributed to either mutation, except among Ashkenazi Jews, who have a 1 in 40 chance of carrying a mutated BRCA gene (a rate 10 times higher than that of the general population).
- BRCA-positive women have options apart from mastectomy, particularly if they’re younger than 40 years and aiming to have children.
- Women should be tested for the mutations only if they meet criteria that include a strong family history for BRCA-related cancers.

The media coverage fell short, Offit said, by failing to highlight a more urgent priority for BRCA-positive women that the public’s obsession with Jolie’s mastectomy overshadowed: oophorectomy, or removal of the ovaries. Early-stage breast tumors can be easily detected with routine surveillance, but this isn’t an option for ovarian cancers deep in the body, which are often diagnosed late in their development.

“We find roughly four microscopic ovarian cancers for every 100 oophorectomies performed in response to genetic screening,” Offit said. “That’s as close to curative surgery as we can get in the cancer-prevention business.”

Oophorectomy reduces risk for breast cancer presumably because of the resulting decrease in estrogen; however, the estrogen–breast cancer link is complex. For example, replacing estrogen (without progesterone) in women who have had both ovaries and uterus removed preventively is not believed to increase breast cancer risk substantially. Also, Offit’s analysis showed that the major breast cancer–preventive role for oophorectomy is for BRCA2 and not BRCA1 mutation carriers, presumably because many more BRCA2 mutation carriers develop estrogen receptor–positive breast cancers. Jolie, whose breasts were cancer free when removed, didn’t mention oophorectomy in her editorial. She has since announced that she will have the procedure.

“We don’t want to scare women away,” Domchek said. “In many cases, there’s no rush. Jolie’s editorial cites an upper-bound lifetime risk of 87% from a BRCA1 mutation, but cancer risks for these women also grow with age. A younger BRCA-positive woman in her 20s, for instance, can have risks as low as 5% in any given year.”

But for younger women, child rearing can be a priority that also limits preventive options in the near term. According to Nancy Davidson, MD, director of the University of Pittsburgh Cancer Center, raloxifene in the BRCA-positive setting is indicated only for postmenopausal women, whereas tamoxifen—which is also antiestrogenic—can interfere with a healthy pregnancy. That leaves surveillance as the sole option. Offit pointed out that MRI detects breast tumors in BRCA-positive women with a sensitivity approaching 90%, compared with 50% for mammography. Consensus surveillance strategies for high-risk women aren’t available. But Domchek cited a recent study presented at the American Society of Clinical Oncology’s annual meeting last June, showing that...
No Clear Link Between Passive Smoking and Lung Cancer

**By Judy Peres**

A large prospective cohort study of more than 76,000 women confirmed a strong association between cigarette smoking and lung cancer but found no link between the disease and secondhand smoke.

“The fact that passive smoking may not be strongly associated with lung cancer points to a need to find other risk factors for the disease [in nonsmokers],” said Ange Wang, the Stanford University medical student who presented the study at the June