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Battling Cancer Again

BY TERESA MCUSIC

Some treatments can cause secondary cancers years or decades later.

Hearing the words *you have cancer* is difficult, but hearing them a second time can be devastating.

Kari Dudley, 38, a vice president in financial services in Boston, heard those words two years ago after being treated for early-stage Hodgkin disease in 1995 with mantle field radiation—radiation to the neck, chest, and underarm lymph nodes.

“I remember I was doing a happy dance that I didn’t need chemo,” she recalls.

But in a twist that is still rare but increasing as cancer patients live longer, Dudley’s cancer treatment was probably the catalyst that caused her stage 2 breast cancer 12 years later. Indeed, Dudley had seen studies about mantle field radiation causing treatment-based, or secondary, cancers and had been diligent in her follow-ups. In fact her breast cancer was discovered while she was enrolled in a secondary cancers study sponsored by the Lance Armstrong Foundation.

The mother of two young girls, Dudley decided to treat the new cancer aggressively and had a bilateral mastectomy and chemotherapy.



Kari Dudley with her daughters, Isabella (left) and Chloe. Photo by Jim Dwyer.

The Second Cancer Conundrum

Not to be confused with a recurrence of the primary tumor, being diagnosed with a new cancer can be either a second cancer, meaning it is coincidental and in no way connected to treatment for the first diagnosis, or a secondary cancer, one that may have been caused (or whose risk may have been increased) by treatment for the initial cancer.

According to statistics gathered in 2002, of the new diagnoses reported to the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program, 16 percent were either a recurrence of the primary cancer or a second malignancy.

"If you go back 25 or 30 years, it was just 5 percent," says Alfred Neugut, MD, PhD, a researcher and professor of medicine and epidemiology at Columbia University. "They are increasing because people are living to get them."

Second cancers occur for a variety of reasons, the majority not related to past cancer treatment. For example, it is well known that breast cancer survivors with a BRCA mutation are more susceptible to ovarian cancer, and current or former smokers who have survived other cancers may have an increased risk of lung cancer.

And, despite research, linking treatment to another cancer is a difficult task, says Andrea Ng, MD, a researcher on long-term effects of lymphoma treatment and associate professor of radiation and oncology at Harvard Medical School.

"It's hard to prove," she says. "There is no good way to know if a breast cancer is caused from a previous treatment or something that would develop anyway." Research also shows that the risk of secondary cancers can vary based on the type of primary cancer, age at diagnosis, and type of treatment received.

“ Treatments have been eliminated because the risks of using them are very high. ”

—Alfred Neugut, MD, PhD

Studies tell us the biggest culprits of secondary cancers are high doses of radiation in certain areas and particular types of chemotherapy, such as alkylating agents. Of the two, radiation therapy poses the greatest risk, Neugut says. Radiation can result in solid tumors, usually near the radiation field and especially in younger patients, while some chemotherapy agents may lead to blood cancers such as leukemia. Ng says chemotherapy-linked secondary cancers usually appear within the first 10 years after treatment, while it may take

up to 30 years for a radiation-related solid tumor to emerge.

“Cancer treatments have been heavily studied,” Neugut says. “There are certain patterns, and treatments have been eliminated because the risks of using them are very high.”

According to Ng’s research published in a 2002 issue of *Blood*, among 1,319 patients with Hodgkin disease, 181 secondary malignancies and 18 third malignancies were identified. The risk of a secondary cancer was significantly higher for those patients who received combined chemotherapy and radiation therapy compared with those who received only radiation, and the risk increased with increasing radiation field size in the patients who received both treatment modalities.

Ng’s latest review on secondary cancers, published in the April 2008 edition of the journal *Hematology/Oncology Clinics of North America*, concluded that Hodgkin disease patients treated with chemotherapy and radiation before current treatment practices were put in place, have an increased risk of secondary cancers, including leukemia, breast cancer, and lung cancer.

But, she notes, today’s standard of care for Hodgkin disease includes different chemotherapy drugs, along with lower doses and smaller fields of radiation, which should lower the risk of secondary malignancies.

One of the newest studies to look at secondary cancers, a Dutch study published in December 2008 in the *Journal of Clinical Oncology*, compared the risk of cancer in the opposite (contralateral) breast in women who were treated between 1970 and 1986 with radiation either after a lumpectomy or after a mastectomy. The authors noted that post-lumpectomy radiation likely resulted in a much higher dose to the opposite breast than post-mastectomy radiation.

““ Patients we treated here 10 or 15 years ago are surprised to hear they have an increased risk of cancer. ””

—Andrea Ng, MD

The study found that radiation did not significantly increase the overall risk of a new cancer in the opposite breast in either group. However, women treated with post-lumpectomy radiation before age 45 had a 1.5-fold increased risk of contralateral breast cancer compared with women who had undergone post-mastectomy radiation. These younger women who also had a strong family history of breast cancer had a 3.5-fold increased risk. The authors noted, however, that the improvement of radiation techniques over the past few decades has reduced the risk of contralateral breast cancer.

Avoiding the Second Time Around

Lowering the dose or administering fewer cycles of chemotherapies now known

to cause secondary cancers are strategies used currently to avoid therapy-related cancers.

“For most aggressive cancers—lung, gastrointestinal, breast—the foremost goal remains to cure the first cancer,” Ng says. “For those cancers that we have a high cure rate, such as Hodgkin’s, testicular, and certain pediatric cancers such as acute lymphoblastic leukemia, there are ongoing efforts to modify or reduce treatment to avoid secondary cancers.”

Such findings have led doctors to pay more attention not only to who is getting a therapy-related cancer, but also when and why—with treatment changing as a result. But it’s still important to treat adequately, Neugut says.

“Ultimately if you have a person in front of you and they have a risk of dying [from cancer] that is 80 percent, and you have a one in 100 chance of [secondary] malignancy during the rest of their life, that’s a trade-off I’ll take any day of the week,” he says.

Ng emphasizes the importance of screening for patients who have received treatment in the past. Indeed, a study published in January in the *Journal of the American Medical Association* looked at 551 women ages 25 to 50 who were treated with chest radiation for childhood cancer before age 21. Despite having a significantly higher risk for breast cancer, among the subgroup of 296 women ages 25 to 39, only 108 women—or 36.5 percent—had received a screening mammogram in the past two years. The investigators noted that by age 45, approximately 12 to 20 percent of women treated with moderate- to high-dose chest radiation will have breast cancer.

“Patients we treated here 10 or 15 years ago are surprised to hear they have an increased risk of cancer,” Ng says. “We advocate going to a cancer center for follow-up, or educate your doctor about your risks.”

Georgene Van Seggern, 62, of New Jersey was diagnosed with acute myeloid leukemia, or AML, six years after receiving chemotherapy for multiple myeloma. After a stem cell transplant using cord blood to treat the AML, Van Seggern is now cancer-free and diligent about her checkups.

“I may put off other things, but I never miss getting my six-month blood work done.”

Ng says survivors should ask their physician for their treatment summary and a survivorship care plan that includes monitoring for long-term effects such as secondary cancers (see [“Mapping the Journey”](#) from the Winter 2008 issue). She also suggests survivors focus on a healthy lifestyle, don’t smoke, limit alcohol consumption, and use sun protection.

“Some patients walk away after five-year checkup and don’t go to see anybody for years,” Ng says. “They should see a health care provider once a year at least.”