Penn scientist's vaccine shows promise against early form of breast cancer

By Marie McCullough
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One year ago, Shelley Dodt received a thrilling e-mail from her University of Pennsylvania breast surgeon:

Shelley,

Your pathology is completely benign. No evidence of residual DCIS. Happy Thanksgiving to you and your family.

Brian

Dodt, now 56, of Palm City, Fla., had received Brian J. Czerniecki's experimental vaccine to treat her early-stage breast cancer, called DCIS, before having surgery to remove the cancer. The pathologist who examined the excised tissue under a microscope could not find any malignant cells. Revved by the vaccine, her immune system had wiped out the cancer.

Few other patients have responded so completely to the vaccine, and no one can yet say whether the protective effect will decline over time. Still, in a field littered with failures, Czerniecki's team has found a way to make the concept - a therapeutic cancer vaccine - work well.

Any patient would have been grateful; Dodt was also inspired by her unpretentious, teddy-bearish doctor and his team.

The former marketing executive soon joined forces with another patient-turned-devotee, the Olympic figure-skating coach Uschi Keszler of Aston. To date, their Delaware County nonprofit, Pennies in Action, has raised more than $200,000 for the ongoing vaccine trials - a much-needed supplement to federal funding.

The women have an infectious - and sometimes hyperbolic - enthusiasm.

"Uschi and I just live for the day that the last mammography machine is pushed over the cliff," Dodt said Monday, back at Penn for one of the semiannual checkups she will have for five years.

Tough to detect

It was vanity, Dodt said, that led to her diagnosis. The lithe blonde hated the underarm fat that bulged over...
the left side of her bra when she worked out in a sleeveless leotard.

After the offending flesh was removed in August 2009, a routine pathology exam revealed malignant cells lining her milk ducts. Left alone, some DCIS - ductal carcinoma in situ - will progress and break through the duct walls, invading surrounding breast tissue. To be safe, DCIS is treated like invasive cancer - with a lumpectomy or mastectomy followed by radiation.

Years ago, DCIS was almost never caught, because it can't be felt as a lump. The advent of mammography in the 1970s enabled detection of the tiny calcifications that are often a sign of DCIS.

Now it is diagnosed in 60,000 women a year, and counting. That's 20 percent of all newly found breast cancers.

But mammography often misses DCIS. Dodt's, for example, never showed up on repeated X-rays and MRI scans.

Dodt underwent a lumpectomy and was scheduled for radiation when she read the pathology report. It was not good. The lump did not have "clean margins" - a border of cancer-free tissue - so she needed yet another operation. And her DCIS was loaded with something called HER2/neu.

She turned to the Internet to learn more.

HER2 is a growth protein known to make invasive cancers aggressive and likely to recur despite treatment. Only about a quarter of invasive cancers "overexpress" HER2, but 40 percent of DCIS cases do.

By serendipity, Dodt found a just-published journal article that said HER2 could be used to predict whether DCIS would become invasive. That finding was based on the first, small trial of a vaccine designed to attack exactly what she had - HER2-positive DCIS.

At 7:42 p.m. on Aug. 26, 2009, she e-mailed the key author, peppering him with questions.

"Please advise if you are able to take the time," she wrote.

Six minutes later, Czerniecki responded.

Over the next few hours, as they exchanged e-mails, Dodt learned that patients were being recruited for a second trial of the vaccine, and she asked to be considered.

Czerniecki told her that she was not eligible. After all, she had already had a lumpectomy, so she had no DCIS left for the vaccine to target.

Dodt clarified that because she did not have clean margins, she needed more surgery. "I want this vaccine," she e-mailed at 9:48 p.m. "I saw your chart and can see you are achieving excellent responses. I want this disease decimated badly."

At 10:20 p.m., Czerniecki responded: "If you need additional surgery, you are eligible."

How the trial works

Previous patients had all come from the Philadelphia area because the trial requires numerous trips to the Hospital of the University of Pennsylvania.
First, the patients undergo an hours-long procedure to remove their blood’s dendritic cells - star-shaped messenger cells that latch onto suspicious proteins, then present the threatening molecules to infection-fighting parts of the immune system.

In lab dishes, the dendritic cells are multiplied and exposed to HER2.

The resulting tailor-made vaccine is injected back into the patient’s lymph nodes in four weekly doses. After a lumpectomy or mastectomy, the patient's blood and breast tissue undergo a battery of sophisticated analyses.

Many similar therapeutic cancer vaccines have been in trials in recent years with little success. Largely, this is because they must first be tested in terminally ill patients - people whose immune systems have been ravaged.

"DCIS patients are good candidates for testing," Czerniecki wrote in 2007, "because they are otherwise healthy."

Indeed, the first trial was encouraging. Of 27 patients, 90 percent showed measurable immune response. In half of the patients, their DCIS cells were stripped of the target HER2.

In five patients - 19 percent - the DCIS was completely gone.

To try to boost that percentage, the second trial would give six weekly doses, and some patients would get the injections in both lymph nodes and the breast that had DCIS.

**Not too busy to soothe**

Like most clinician-researchers, Czerniecki is a multitasker who needs little sleep.

Fourteen-hour workdays are common. Then he goes home to "hang out" with his wife and two teenage children, or coach their soccer teams. At 9 p.m., he hits the gym. Afterward, he gets on the computer or the BlackBerry.

"Sometimes patients e-mail me at midnight," he said. "If I can send a few words by e-mail, it's quicker than a call."

Again and again, his words calmed Dodt.

In September last year, she panicked that a mammogram had shown microcalcifications - in her other breast. Before biopsies could evaluate these "calcs," she e-mailed Czerniecki: "Will having it in two places mean I would need a double mastectomy?"

He responded that calcs were not always a sign of malignancy, adding: "Get the biopsies done. If you have more DCIS it will not knock you out of the trial."

The calcs were benign.

Last November, Dodt fretted about living with "the stress" of the fear of recurrence.

"I am 55 years old and really don't have the need for the spectacular breasts younger women are demanding," she e-mailed. "If I did have the double mastectomy, and having the protection of the HER2/neu vaccine, what would my chances be for a breast cancer-free life?"

"Shelley," he responded, "you do not need bilateral mastectomy. See what you have in the remainder at lumpectomy, then go from there."

That postvaccination lumpectomy led to last Thanksgiving's "no residual DCIS" e-mail, for which she will be forever grateful.

'The Olympic attitude'

Even before that e-mail, Dodt asked Czerniecki how she could promote his research. "Go see Uschi," he responded.

Raised in what was then West Germany, Keszler became that nation's figure-skating champion in 1965. The next year, at 16, she contracted tuberculosis, and spent eight months in a sanitarium.

She moved to the United States at 18, married, had a son, and became internationally known for coaching other champions, notably the Olympic medalists Brian Orser and Elvis Stojko.

Czerniecki treated Keszler five years ago for invasive breast cancer, not DCIS. She was captivated when she learned of his vaccine research - and outraged that the vagaries of federal funding had left the first trial with a considerable shortfall.

"I come from the sports world," she said. "It would be the same as funding someone through nationals and not for Olympics."

Czerniecki put it this way: "She's very driven. I think she feels like we're not getting places fast enough. I think she takes the Olympic attitude, where you get people together and train them and take up the cause."

Keszler set up Pennies in Action three years ago. In Dodt, she found a like-minded crusader, eager to set up the "Florida chapter."

Through their website, YouTube posts, hockey tournaments, dinners, and other fund-raising efforts, they have turned donations - a lot of them spare change - into laboratory supplies and sometimes even paychecks for Czerniecki's team.

Despite encouraging results, the vaccine research has a long way to go. Only nine patients have been enrolled in the second trial, with a goal of 57. A third, much bigger, trial will be required.

Still, Czerniecki believes the technology can be applied to fight other breast-cancer-promoting proteins - and other types of cancer.

His fans have absolutely no doubt.

"Nobody believed that TB could be conquered, but it was," said Keszler. "This vaccine is writing a new page in history."

More Information

About the vaccine trial: At www.clinicaltrials.gov, search for DCIS vaccine
http://www.printhis.clickability.com/pt/cpt?action=cpt&title=Penn+scientist%27s+vaccine+shows+promise+against+early+form+of+breast+cancer+&pr...