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Study Suggests Some Cancers May Go Away

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Cancer researchers have known for years that it was possible in rare cases for some cancers to go away on their own. There were occasional instances of melanomas and kidney cancers that just vanished. And neuroblastoma, a very rare childhood tumor, can go away without treatment.

But these were mostly seen as oddities — an unusual pediatric cancer that might not bear on common cancers of adults, a smattering of case reports of spontaneous cures. And since almost every cancer that is detected is treated, it seemed impossible even to ask what would happen if cancers were left alone.

Now, though, researchers say they have found a situation in Norway that has let them ask that question about breast cancer. And their new study, to be published Tuesday in *The Archives of Internal Medicine*, suggests that even invasive cancers may sometimes go away without treatment and in larger numbers than anyone ever believed.

At the moment, the finding has no practical applications because no one knows whether a detected cancer will disappear or continue to spread or kill.

And some experts remain unconvinced.

“Their simplification of a complicated issue is both overreaching and alarming,” said Robert A. Smith, director of breast cancer screening at the American Cancer Society.

But others, including Robert M. Kaplan, the chairman of the department of health services at the School of Public Health at the University of California, Los Angeles, are persuaded by the analysis. The implications are potentially enormous, Dr. Kaplan said.

If the results are replicated, he said, it could eventually be possible for some women to opt for so-called watchful waiting, monitoring a tumor in their breast to see whether it grows. “People have never thought that way about breast cancer,” he added.

Dr. Kaplan and his colleague, Dr. Franz Porzsolt, an oncologist at the University of Ulm, said in an editorial that accompanied the study, “If the spontaneous remission hypothesis is credible, it should cause a major re-evaluation in the approach to breast cancer research and treatment.”

The study was conducted by Dr. H. Gilbert Welch, a researcher at the VA Outcomes Group in White River Junction, Vt., and Dartmouth Medical School; Dr. Per-Henrik Zahl of the Norwegian Institute of Public Health; and Dr. Jan Maehlen of Ullevål University Hospital in Oslo. It compared two groups of women ages 50 to 64 in two consecutive six-year periods.

One group of 109,784 women was followed from 1992 to 1997. Mammography screening in Norway was initiated in 1996. In 1996 and 1997, all were offered mammograms, and nearly every woman accepted.

The second group of 119,472 women was followed from 1996 to 2001. All were offered regular mammograms, and nearly all accepted.

It might be expected that the two groups would have roughly the same number of breast cancers, either detected at the end or found along the way. Instead, the researchers report, the women who had regular routine screenings had 22 percent more cancers. For every 100,000 women who were screened regularly, 1,909 were diagnosed with invasive breast cancer over six years, compared with 1,564 women who did not have regular screening.

There are other explanations, but researchers say that they are less likely than the conclusion that the tumors disappeared.

The most likely explanation, Dr. Welch said, is that “there are some women who had cancer at one point and who later don’t have that cancer.”

The finding does not mean that mammograms caused breast cancer. Nor does it bear on whether women should continue to have mammograms, since so little is known about the progress of most cancers.

Mammograms save lives, Dr. Smith said. Even though they can have a downside — most notably the risk that a woman might have a biopsy to check on an abnormality that turns out not to be cancer — “the balance of benefits and harms is still considerably in favor of screening for breast cancer,” he said.

But Dr. Suzanne W. Fletcher, an emerita professor of ambulatory care and prevention at Harvard Medical School, said that it was also important for women and doctors to understand the entire picture of cancer screening. The new finding, she said, was “part of the picture.”

“The issue is the unintended consequences that can come with our screening,” Dr. Fletcher said, meaning biopsies for lumps that were not cancers or, it now appears, sometimes treating a cancer that might not have needed treatment. “In general we tend to underplay them.”

Dr. Welch said the cancers in question had broken through the milk ducts, where most breast cancers begin, and invaded the breast. Such cancers are not microscopic, often are palpable, and are bigger and look more ominous than those confined to milk ducts, so-called ductal carcinoma in situ, or DCIS, Dr. Welch said. Doctors surgically remove invasive cancers and, depending on the circumstances, may also treat women with radiation, chemotherapy or both.

The study’s design was not perfect, but researchers say the ideal study is not feasible. It would entail screening women, randomly assigning them to have their screen-detected cancers treated or not, and following them to see how many untreated cancers went away on their own.

But, they said, they were astonished by the results.

“I think everybody is surprised by this finding,” Dr. Kaplan said. He and Dr. Porzsolt spent a weekend reading and re-reading the paper.

“Our initial reaction was, ‘This is pretty weird,’ ” Dr. Kaplan said. “But the more we looked at it, the more we were persuaded.”

Dr. Barnett Kramer, director of the Office of Disease Prevention at the National Institutes of Health, had a similar reaction. “People who are familiar with the broad range of behaviors of a variety of cancers know spontaneous regression is possible,” he said. “But what is shocking is that it can occur so frequently.”

Although the researchers cannot completely rule out other explanations, Dr. Kramer said, “they do a good job of showing they are not highly likely.”

A leading alternative explanation for the results is that the women having regular scans used hormone therapy for menopause and the other women did not. But the researchers calculated that hormone use could account for no more than 3 percent of the effect.

Maybe mammography was more sensitive in the second six-year period, able to pick up more tumors. But, the authors report, mammography’s sensitivity did not appear to have changed.

Or perhaps the screened women had a higher cancer risk to begin with. But, the investigators say, the groups were remarkably similar in their risk factors.

Dr. Smith, however, said the study was flawed and the interpretation incorrect. Among other things, he said, one round of screening in the first group of women would never find all the cancers that regular screening had found in the second group. The reason, he said, is that mammography is not perfect, and cancers that are missed on one round of screening will be detected on another.

But Dr. Welch said that he and his colleagues considered that possibility, too. And, he said, their analysis found subsequent mammograms could not make up the difference.

Dr. Kaplan is already thinking of how to replicate the result. One possibility, he said, is to do the same sort of study in Mexico, where mammography screening is now being introduced.

Donald A. Berry, chairman of the department of biostatistics at M. D. Anderson Cancer Center in Houston, said the study increased his worries about screenings that find cancers earlier and earlier. Unless there is some understanding of the natural history of the cancers that are found — which are dangerous and which are not — the result can easily be more treatment of cancers that would not cause harm if left untreated, he said.

“There may be some benefit to very early detection, but the costs will be huge — and I don’t mean monetary costs,” Dr. Berry said. “It’s possible that we all have cells that are cancerous and that grow a bit before being dumped by the body. ‘Hell bent for leather’ early detection research will lead to finding some of them. What will be the consequence? Prophylactic removal of organs in the masses? It’s really scary.”

But Dr. Laura Esserman, professor of surgery and radiology at the University of California, San Francisco, sees a real opportunity to figure out why some cancers go away.

“I am a breast cancer surgeon; I run a breast cancer program,” she said. “I treat women every day, and I promise you it’s a problem. Every time you tell a person they have cancer, their whole life runs before their eyes.

“What if I could say, ‘It’s not a real cancer, it will go away, don’t worry about it,’ ” she added. “That’s such a different message. Imagine how you would feel.”