PREGNANCY

Delivery from breast cancer

Growing evidence shows that pregnant patients can beat breast cancer without endangering the unborn child.

BY MICHAEL EISENSTEIN

When a pregnant woman is confronted with a diagnosis of breast cancer, the combined burden can seem like too much to bear. "If the first thing a physician says to a patient is, 'You must choose between yourself and the pregnancy', that's a mistake, and we know it," says Fedro Peccatori, a specialist in pregnancy-associated cancers at the European Institute of Oncology in Milan, Italy. Nevertheless, it is understandable that many doctors do not fully understand how pregnancy affects cancer progression or treatment options, as many aspects of this relationship are still coming into focus.

About 1 in 3,000 pregnancies is associated with a breast cancer diagnosis. The numbers are small but, as more women delay childbearing to an age where the risk of breast cancer is greater, these numbers are likely to increase. One study, based on a registry of Norwegian patients, showed a 2.5% annual increase in the risk of cancer during pregnancy, with breast cancer the most common diagnosis[1].

Numerous studies have reported that pregnancy-associated breast tumours are larger and more aggressive, and that patients tend to fare worse overall than women with breast cancer who are not pregnant. But the reality is more complex.

In most studies, this increased frequency of late-stage tumours is a product of delayed diagnosis. During pregnancy, the breasts undergo physiological changes that can mask cancerous growths. "It can be difficult to differentiate lumps in the breast that formed because of the pregnancy from true neoplastic nodules," says Peccatori. This increase in breast tissue density also makes mammograms difficult to interpret (see 'A dense issue', page S60).

Another issue is that 'pregnancy-associated breast cancer' is inconsistently defined across studies, and can include tumours diagnosed up to a year after giving birth. Many experts are concerned that this might skew the outcome data. Elyce Cardonick, a specialist in high-risk obstetrics at Cooper University Hospital in Camden, New Jersey, suggests using a shorter time frame to exclude tumours that develop after pregnancy. "A tumour detected one year post-partum could have formed after pregnancy," she says, "but maybe not one detected within six months of delivery."

As a result, the specific risks of pregnancy-associated breast cancer are ambiguous. When pregnant patients are matched to non-pregnant counterparts, based on parameters such as age and tumour stage, differences in tumour characteristics largely disappear. But a handful of studies, including recent work by Peccatori's team[2], indicate a small but statistically meaningful increase in the risk of breast cancer recurrence in patients diagnosed during pregnancy.

Fortunately, experts in cancer during pregnancy have found that most standard therapeutic options should remain on the table. "We have quite good data," says Frédéric Amant, a gynaecological oncologist at the Catholic University in Leuven, Belgium, "and I think it becomes more and more difficult to justify termination of pregnancy." For example, surgery can safely be performed after the first trimester. Radiotherapy can be delivered as a follow-up at a reasonably low risk to the developing fetus during the second trimester; patients in late pregnancy should delay radiotherapy until after delivery.

A. DE WULF

A healthy mother and baby after chemotherapy.

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Most of the chemotherapeutic agents typically given as an adjunct to surgery also remain in play. "We want to give pregnant women the same chemotherapy as non-pregnant women," says Amant. "The best chance for the best prognosis is to give the standard treatment." Chemotherapy should be avoided during the first trimester; however, by 15 weeks, the organs have developed to a stage at which birth defects are not a serious concern. Only a few drugs — most notably the oestrogen-receptor blocker tamoxifen and the antibody-based drug trastuzumab (Herceptin) — have proven fetal health risks, and doctors are advised not to use these until after delivery.

Long-term studies indicate that children exposed to chemotherapy *in utero* do not seem to experience significant ill effects as they grow older. The most recent study was published by Amant and colleagues[3], who examined a group of children up to 18 years of age. They concluded that anticancer treatments had no meaningful effect on physiological development or cognitive indicators. In fact, exposure to chemotherapy may be less detrimental than inducing early delivery to minimize drug exposure. "Children behind in development were mostly concentrated in the group that was delivered prematurely," says Cardonick.

But the rarity of pregnancy-associated breast cancer makes it difficult to draw confident conclusions about long-term risks to children's health. Multi-institutional registries, such as Amant's Cancer and Pregnancy project in Europe and Cardonick's Pregnancy & Cancer Registry in the United States, should help. These groups are looking to turn isolated reports into statistically robust, actionable data, by collecting as much information as possible about the recovery and long-term health of both mothers and children after different treatments during pregnancy. "It's very important to learn from our previous patients what to do with the next patients," says Peccatori.

In the meantime, doctors hope the existing data will reassure women facing a breast cancer diagnosis that they are likely to be able to carry their pregnancies to term. These patients might also benefit from organizations that connect them with mothers who have survived breast cancer. One such network is Hope for Two, based in Amherst, New York, for which Cardonick is an adviser. "Talking to somebody who had breast cancer might be helpful," says Cardonick, "but it's nothing like talking to somebody who has gone through the same thing and successfully delivered her baby." ■

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1. Stensheim, H. *et al. J. Clin. Oncol.* **27**, 45–51 (2009).
2. Azim, H. A. Jr *et al. Acta Oncol.* doi: 10.3109/0284186X.2011.636069 (16 December 2011).
3. Amant, F. A. *et al. Lancet Oncol.* **13**, 256–264 (2012).