

Chapter 35

Discussing Fertility Preservation with Breast Cancer Patients

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Introduction

Approximately 180,000 women are diagnosed with breast cancer each year. Of these patients, over 16,000 are younger than age 45 [1]. Receiving a diagnosis of breast cancer is difficult regardless of the patient's age. Simultaneously, the impact of this diagnosis for younger premenopausal patients may be particularly traumatic as the implications of the diagnosis may have an added morbidity of fertility loss. Navigating the issue of fertility in the midst of a new cancer diagnosis is complex for both the patient and the physician. This complexity primarily stems from the relatively short time frame available to organize a plan of care that encompasses all the patient's needs, both oncologically and for fertility preservation. The emergence of the field of oncofertility has enabled a more streamlined approach to the newly diagnosed breast cancer patient who has a desire for fertility preservation. Through the interdisciplinary effort of reproductive specialists in cooperation with oncologists, young breast cancer patients are now meeting the goals of cancer treatment with a greater hope for preserved fertility during survivorship.

There are several different objectives to be met during the initial consultation for a new breast cancer patient interested in fertility preservation. At the outset, the patient's general level of anxiety must be assessed and reassurance provided. For patients with a great deal of diagnosis-related anxiety, the ability to process and retain new information can be very difficult. Accordingly, the amount of new information conveyed to the patient must take place in a stepwise fashion that suits the patient's capacity to participate in this important conversation. Typically, at the time of presentation, the patient has already undergone several radiographic and interventional diagnostic tests. Often, a discussion of these tests and their findings is reviewed at the outset of the consultation. This helps to ensure that the patient and the physician share an understanding of the diagnosis and any additional tests that may be necessary to establish a cancer treatment plan. The patient's medical history is then reviewed in detail. This history includes the patient's prior illnesses or hospitalizations, medications, family history of cancer, and a precise history of hormone exposures including birth control pills, fertility treatments, and supplemental estrogen therapy. Additional information is obtained about the onset of menarche, as well as the patient's childbearing and lactation history. It is during this time that the subject of fertility preservation may be initially discussed. Often a simple question, such as "Were you thinking about having a child?" or "Were you planning to have any more children?" can help get the patient to begin thinking about her fertility.

The patient is then examined and the conversation typically refocuses to the plan for cancer treatment. Once the initial cancer treatment plan is outlined, which often includes a combination of surgery, chemotherapy, and radiation, the issue of fertility preservation is then readdressed. By this point in the visit, the physician may either know or can reasonably speculate on the likelihood that the patient will require chemotherapy as part of her care. The inclusion of chemotherapy in the treatment plan poses the greatest fertility risk for breast cancer patients. Once the patient is informed of the potential need for chemotherapy, she may then be more focused on the immediate threat to her fertility, unlike the patient who will not require this component of breast cancer management.

When a patient with a fertility threat is interested in options for preservation, often a detailed discussion of the potential options for fertility preservation is held at the end of the initial breast cancer consultation. The level of detail in which these options are discussed is entirely dependent upon the patient's ability and desire to obtain more complex information while establishing a cancer treatment plan. While it is at times difficult to address an additional critical subject after discussing the cancer treatment plan, the sooner the patient's fertility issues are addressed, the greater the chance that the fertility preservation measures will occur without any need for delaying cancer therapy. Subsequent to completion of the initial visit with the oncologist, if possible, the patient should undergo counseling about fertility preservation during a separate encounter with a fertility preservation specialist. If the patient desires this meeting and it can be arranged, the second consultation may occur on the same day as the initial cancer consultation. If the patient has a partner who was not present for the initial cancer consultation, often the fertility preservation consultation will be deferred to include both the patient and her partner.

The significance of a second consultation with a fertility specialist is several fold. Although the oncologist may have the best intentions regarding meeting all of the patient's needs, it is difficult to discern if some bias against fertility preservation measures, in favor of a more simplistic and traditional cancer care plan, may affect the ability of the oncologist to present a balanced approach to fertility preservation options. Simultaneously, the patient may associate the oncologist primarily with cancer management and may not be able to think beyond cancer care to issues of survivorship while in the presence of an oncologist. Meeting separately with the fertility preservation specialist who will be providing the care necessary for fertility preservation allows patients to think about the future and survivorship without simultaneously being faced with the present and the impact of the new cancer diagnosis. While some patients may be ready to meet with the fertility specialist immediately after the cancer consultation, it may be optimal for most patients to have this second consultation a few days after the initial cancer plan is established to allow for time to process new information and to prepare for additional decision making. The appropriate coordination and timeline of these visits should be determined by the patient and the oncologist on an individual basis.

Some young cancer patients will require chemotherapy before surgery due to their more advanced stage at presentation. For these patients, fertility preservation options will take immediate precedence in the patient's overall management plan and will need to be

rapidly facilitated. Most patients undergo surgery as the initial step in their cancer care. For some of these patients, the need for chemotherapy will only be determined after definitive pathologic information is available. Additionally, for those patients whose tumors will undergo advanced genetic assessment to help establish the need for chemotherapy, the time between surgical recovery and the start of chemotherapy can be up to 1 month. This time interval should allow sufficient time for several fertility preservation interventions without disrupting the flow of the cancer treatment plan. It is critical to utilize the window of time prior to the initiation of chemotherapy, not only because this treatment may last from 4 to 6 months and permanently damage fertility but also for some patients, additional treatment may be necessary that may delay potential fertility interventions for up to 1 year. Furthermore, for approximately 70% of patients whose tumors express estrogen receptors, 5 years of anti-estrogen therapy with tamoxifen will be recommended. Although this treatment can potentially be delayed for childbearing, at this point, the optimal regimen is to complete a 5-year course, during which time pregnancy should be avoided. These treatment issues underscore the importance of early discussion about fertility preservation in the establishment of a patient's management plan and the significance of a team of caregivers who are knowledgeable and available to provide the care necessary to allow for the treatment of breast cancer in conjunction with fertility preservation.

Case #1: A Young Patient Who Refused Fertility Preservation

A 37-year-old female patient presented with a 2cm isolated left breast mass located in the upper outer quadrant. The mass was palpable and appeared suspicious on ultrasound, mammogram, and MR imaging. Ultrasound-guided core biopsy of the lesion was performed and the pathology revealed estrogen (ER)-, progesterone (PR)-, and human epidermal growth factor receptor 2 (HER2)-positive disease. The patient was a high-level business executive and competitive athlete. At the patient's initial consultation, she was very anxious to arrange a surgery date. She was interested in the option of breast-conserving surgery with post-operative radiation therapy, which would allow her the quickest recovery time so that she could return to her athletic training. In light of her HER2-positive diagnosis, treatment with chemotherapy was also indicated. Prior to the end of her initial visit, the issue of fertility preservation was discussed with the patient and her husband. The patient said that she was not interested in fertility preservation, stating that she wanted to focus on beginning her cancer treatment and returning to her athletic goals. Subsequent to the patient's first surgery, she was found to have axillary nodal involvement requiring an additional operation. During the consultation for this second surgery the subject of fertility preservation was again addressed with the patient and she refused. Additional counseling with an oncofertility patient navigator was offered, but the patient declined. Subsequent to the patient's second surgery, she began treatment with chemotherapy. Eight months after the initiation of the patient's cancer treatment, she and her husband returned to the surgery clinic for a follow-up appointment. At this point, they stated their desire to start a family. Since the patient began treatment with chemotherapy, she had become amenorrheic. Additionally, she had six additional months of bioimmunotherapy with herceptin remaining in her treatment course, during which time it would not be considered safe to become pregnant or undergo

fertility preservation techniques. At the completion of the patient's herceptin treatment, the patient returned to the clinic for follow-up and remained amenorrheic. She stated regret at not pursuing fertility preservation options prior to the initiation of her cancer treatment. In a few weeks, she was scheduled to begin 5 years of treatment with tamoxifen, during which time pregnancy was also not recommended. At the completion of her tamoxifen therapy, the patient would be nearly 43 years old. She was not comfortable waiting any longer to begin a family and planned to delay treatment with tamoxifen to pursue fertility treatment.

This case highlights the importance of early intervention regarding fertility preservation before the patient begins treatment with systemic therapy. If this opportunity is missed, the potential for the patient to have a biologic child may decrease significantly. Ideally, the patient should meet with two separate experts well versed in fertility preservation options prior to the initiation of treatment, though this may not always be possible to facilitate. It is crucial to be supportive of the patient through the treatment process. Should the patient change her decision regarding her desire for a family, within the framework of the patient's established treatment plan, appropriate counseling should be arranged to help support the patient's wishes.

Case #2: A Young Patient Who Desired Fertility Preservation

A 34-year-old female patient presented with an isolated 3.5cm, firm left breast mass visualized by ultrasound, mammogram, and MRI. Core biopsy of the mass was performed, and ultrasound detected a suspicious left axillary lymph node. Pathology of the primary tumor revealed hormone receptor-negative and HER2-negative infiltrating ductal carcinoma. The left axillary lymph node was also found to be positive for malignancy. Treatment options discussed with the patient and her husband included: timing of chemotherapy, breast conservation versus mastectomy with left axillary dissection, and the use of radiation therapy. The patient opted for primary surgery followed by chemotherapy. The issue of fertility preservation was also discussed, and the patient, who already had two children, strongly expressed her desire for another child.

Shortly after consultation with the surgical oncologist, the patient and her husband met with an oncofertility patient navigator. The patient's case was then presented at multidisciplinary oncofertility rounds attended by the oncofertility team, which included the patient's oncologists, a reproductive endocrinologist, and the patient navigator. During the year prior to the patient's diagnosis, her baseline FSH was found to be 5.0 mIU/ml. The patient then met with the reproductive endocrinologist who discussed fertility preservation options including embryo cryopreservation, oocyte cryopreservation, and ovarian tissue cryopreservation. The patient opted for embryo cryopreservation and was started on oral contraceptive pills due to the early timing of her menstrual cycle at the time of the consultation. She then underwent surgery for her breast cancer and was found to have locally advanced disease. During her 4-week recovery, she completed successful ovarian stimulation and oocyte harvest resulting in the cryopreservation of five embryos. Without any delay in the management of her cancer, the patient then began treatment with chemotherapy. During the patient's treatment, she

often stated that the knowledge that she had preserved her fertility helped her persevere through treatment and served as a great source of comfort to her. Two years after the completion of her treatment, the patient and her husband began thinking about having another child using the patient's banked embryos [2].

This case highlights the relative ease of implementing fertility preservation into the care of breast cancer patients. Critical factors to the success of this practice include early discussion with the patient regarding fertility preservation, patient interest, and establishment of a multidisciplinary oncofertility team that is available to see patients on short notice and is flexible about scheduling visits and procedures in concert with the cancer management plan. Concerns include the reconciliation of a poor prognosis known prior to the initiation of fertility preservation and future plans to have a child in the face of an uncertain life expectancy.

Conclusion

Newly diagnosed young breast cancer patients are faced with several complex decisions regarding both cancer care and fertility preservation during a time of tremendous stress. Patients are often unable to process the impact of a new cancer diagnosis on their fertility at the initial oncology consultation. For this reason, it is critical that the physicians who care for this young cancer population are sensitive to the unique issues inherent to this patient group. It is difficult to predict which patients who initially refuse fertility preservation counseling will have a change of heart subsequent to the initiation of systemic therapy. Counseling must be offered early in the treatment process and on separate occasions to ensure that an appropriate effort has been made to educate the patient about her options. These discussions should be well documented by the health care team members involved.

Ethically, determining how aggressively to pursue the counseling process is challenging. The patient's health care team can never be sure that the patient understands all the risks and benefits of her treatment plan, regardless of how many consultations place. Furthermore, it is ethically challenging to discern if fertility preservation should be offered to breast cancer patients with a known poor prognosis. The implications of producing reproductive material, primarily as a symbol of hope for poor prognosis patients, are far reaching. Just the same, this provision of hope may be a key factor that helps young patients sustain their sense of identity through such a difficult life event. The best practices to capture those patients who will ultimately desire biologic children are actively being examined. Additionally, the appropriateness of patient selection for fertility preservation is also being considered. Currently, fertility preservation counseling is being offered to all patients who are under 45 and to anyone who expresses an interest.

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