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Case Report

CASE REPORT

Fertility preservation before neoadjuvant chemotherapy in a premenopausal breast cancer patient: a case report

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Abstract

Neoadjuvant chemotherapy is now a widely accepted treatment modality for operable breast cancer and therefore fertility preservation is an important component of care for young patients with breast cancer. It is critical that oocyte retrieval is completed without delays in the initiation of neoadjuvant chemotherapy. Here we report the case of a 34-year-old woman who was diagnosed with Stage IIA triple-negative breast cancer and underwent ovarian stimulation for fertility preservation prior to the initiation of neoadjuvant chemotherapy. Oocytes were retrieved and *in vitro* fertilization was conducted before neoadjuvant chemotherapy was started. Upon completion of neoadjuvant chemotherapy, the patient underwent breast surgery. Subsequently, a pathological complete response was achieved. She received a frozen embryo transfer 10 months after breast surgery. The patient became pregnant and delivered a healthy baby.

INTRODUCTION

Neoadjuvant chemotherapy is considered the standard care for operable breast cancer patients, particularly, for patients with triple-negative breast cancer, which is defined as no expressions of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) or HER2-enriched subsets, including locally advanced breast cancer. The commonly used neoadjuvant treatment regimens are well-known for their negative impact on fertility. Specifically, this is due to gonadotoxicity, which importantly may lead to premature ovarian failure [1].

Breast cancer patients of reproductive age should have the opportunity for preserving fertility prior to initiating neoadjuvant chemotherapy. Breast oncologists and surgeons should cooperate with fertility specialists without significantly delaying breast cancer treatment.

The following case is important because a collaborative team effort contributed to neoadjuvant chemotherapy start without breast cancer progress and embryo transfer helped her become pregnant and give birth following breast surgery.

CASE REPORT

In May 2016, a 34-year-old woman, gravida 0, para 0, noticed a lump in her right breast. During physical examination, we identified a 2-cm lump in her right upper breast and absence of axillary lymphadenopathy. Diagnostic mammography detected a mass without speculation. Breast ultrasonography revealed

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Table 1: Summary of breast cancer diagnosis and treatment

Diagnosis and treatment	Results
Mammography	Suspicious abnormality
Breast ultrasound	Suspicious abnormality hypoechoic mass with the size of 22 × 20 mm
Computed tomography	No sign of lymph node and distant organs metastases
Breast MRI	Oval, irregular, rim enhancement, 21 × 16 mm
Needle biopsy	Solid-tubular carcinoma
Clinical stage	IIA (T2N0M0)
Subtype	Triple-negative (ER–, PR–, HER2 1+)
Neoadjuvant chemotherapy	FEC followed by docetaxel
Surgery	Breast-conserving surgery
Radiation therapy after surgery	Whole breast to a dose of 50 Gy in 25 fractions
Adjuvant systemic therapy	No

Table 2: Overview of the clinical course

Time course	Event
Day 0	First visit
Day 14	Diagnosis
Day 28	IVF clinic visit
Day 54	Oocytes retrieved
Day 65	Neoadjuvant chemotherapy starts
8 months after first visit	Surgery
10 months after surgery	Embryo transfer

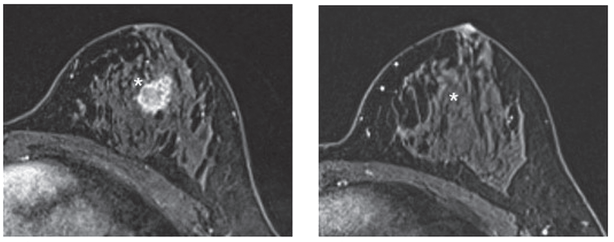

Figure 1: Contrast-enhanced MRI, allowing more detailed information for making the diagnosis of breast cancer, showed a 21-mm mass in the right breast with rim enhancement (left). In the right MRI, there was no sign of breast cancer after neoadjuvant chemotherapy, suggesting a clinical complete response.

a 22-mm hypoechoic solid mass, and contrast-enhanced magnetic resonance imaging (MRI) revealed a 21-mm mass in the right breast with rim enhancement at the 12 o'clock position. Additionally, thoracic and abdominal computed tomography revealed absence of distant organ metastases and no significant enlargement of the lymph nodes, including in the axilla. Following histological examination, the right breast's tumor was confirmed as Grade 3 invasive ductal carcinoma. Immunohistochemistry performed on the primary breast cancer confirmed HER2 1+, negative ER and negative PR. Notably, right axillary lymph node biopsy confirmed absence of breast cancer metastasis (i.e. Stage IIA [T2N0M0]) (Table 1). The patient had a preference for fertility preservation. Consequently, she visited an *in vitro* fertilization (IVF) clinic prior to being treated with neoadjuvant chemotherapy. The goal was to undergo ovarian stimulation using letrozole and human menopausal gonadotrophin. Twenty-six days after the initial visit to the clinic, a total of 10 oocytes were retrieved as the clinical course (Table 2). IVF was performed with her oocytes, resulting in six embryos of good quality for embryo cryopreservation following embryo transfer. Eleven days later, the patient initiated neoadjuvant chemotherapy. Specifically, she underwent four cycles of 5-FU, epirubicin and cyclophosphamide (FEC), followed by four cycles of docetaxel every 3 weeks. Figure 1 indicates the disappearance of breast cancer signs in response to neoadjuvant chemotherapy. Subsequently, breast-conserving surgery and sentinel lymph node biopsy were performed. Histological therapeutic effect was pathological complete response. Standard radiation therapy after breast-conserving surgery was provided, and adjuvant systemic therapy was not provided (Table 1). The frozen embryo transfer was performed 10 months after breast surgery once initial breast cancer treatments were completed and periodical menstruation was recovered (Table 2). The patient went on to achieve pregnancy with only one transfer in hormone replacement cycles and live birth after 40 weeks of gestation.

DISCUSSION

To date, for a number of reasons, there is an increasing trend toward delaying the first pregnancy to 30–40 years of age. Reportedly, this tendency is concordant with an increasing incidence of breast cancer in women who have not yet completed their family [2]. Unfortunately, neoadjuvant chemotherapy or adjuvant chemotherapy regimens commonly used in breast cancer treatment can lead to premature ovarian failure due to their cytotoxic effects on germ cells [3, 4]. Therefore, fertility preservation in breast cancer survivors of reproductive age has become an important issue regarding quality of life.

To date, numerous potential options are available, including all available assisted reproductive technologies (i.e. IVF and embryo transfer, *in vitro* maturation, oocyte and embryo cryopreservation and cryopreservation of ovarian tissue) [5–10]. Currently, embryo cryopreservation represents the most established fertility-preservation strategy. Notably, it provides a 25–35% chance of pregnancy [2, 11]. Additionally, oocyte freezing can be considered an alternative for single parents and for those who do not wish for a sperm donor.

In a systematic review and meta-analysis conducted by Yu *et al.* [12], the authors found that breast cancer patients should start adjuvant chemotherapy with no more than an 8-week delay from the planned initiation, which is probably within 4 weeks after surgery. Thus it is important for fertility preservation procedures to be performed without causing a significant delay in cancer treatment. For breast cancer patients undergoing neoadjuvant chemotherapy, there is no evidence that a longer time prior to treatment is associated with worse survival. Therefore, the safety and outcome of fertility preservation prior to neoadjuvant chemotherapy should be evaluated from a diagnosis–treatment duration perspective in the future. Letourneau *et al.* [13] reported that in their retrospective study, the average time from breast cancer diagnosis to chemotherapy start after ovarian stimulation was 38.1 days. However, in the present case, the time from diagnosis to chemotherapy start was 51 days. The reason why there was a delay in this case, compared with Letourneau's study, was that it took as many as 14 days for our patient to visit the IVF clinic after diagnosis for some reason. Therefore, it is important how quickly patients visit the IVF department or

clinic with enough information about breast cancer and fertility preservation to receive breast cancer treatment without a significant delay.

Breast cancer patients who receive neoadjuvant chemotherapy tend to have higher recurrence risk than those who do not. However, the range of time for initiation of neoadjuvant chemotherapy may be shorter than the duration from surgery to initiation of adjuvant chemotherapy. As a consequence, a collaborative team effort is required. The ultimate goal is to effectively communicate the pros and cons of the various modalities available, treatment's effectiveness, the possible long-term risks, the cost of intervention, support in patients' concerns and treatment planning. Fertility preservation process should start after the diagnosis of breast cancer without a delay in the initiation of neoadjuvant treatment, which becomes a standard care of operable breast cancers.

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CONFLICT OF INTEREST STATEMENT

None declared.

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ETHICAL APPROVAL

No specific ethical approval was required.

CONSENT

Written informed consent was obtained from the patient for the submission of this manuscript.

GUARANTOR

R.M. is the guarantor of this article.

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