CASE REPORT

Dilemmas and Difficulties in Dealing with Receptor-positive Breast Cancer Patients Seeking Fertility Care: A Case Report!

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Abstract

Aim: Addressing the fertility preservation needs of breast cancer patients with receptor-positive presents considerable dilemmas and difficulties.

Case description: Presenting a case of a 35-year-old unmarried female with receptor-positive breast malignancy who was referred for fertility preservation. Counseling regarding remote risk with controlled ovarian stimulation using antagonist protocol was done. Antiestrogen therapy with letrozole was added to minimize the risk with supraphysiologic estrogen levels. Five mature metaphase II (MII) oocytes were retrieved and cryopreserved for future use.

Conclusion: Oocyte cryopreservation in unmarried cancer patients is an acceptable option. The addition of antiestrogen-like letrozole is advisable in estrogen receptor-positive cases. Fertility concerns of young patients should be addressed with a multidisciplinary approach.

Keywords: Breast cancer, Case report, Fertility preservation, Oocyte cryopreservation, Oncofertility, Receptor.

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Introduction

Despite cancer, all young females desire to conceive, with the expectation, to deliver a healthy child. Cancer incidence in women of reproductive age is around 7%.[1] Cancer survival has improved with advancements, so fertility concerns must be addressed. Young patients diagnosed with breast cancer have delayed family planning due to disease process, career, or social reasons.[2] Gynecologists, oncologists, and healthcare workers are encountering more cases of pregnancies after breast cancer treatment.[2] All cancer patients should be counseled for fertility preservation and those who are considering such therapies should be rapidly referred to fertility specialists. Established cryopreservation techniques to preserve fertility include freezing of embryos and gametes.[3] With appropriate pretreatment planning and intervention, future biological parenthood is possible. Women treated with chemotherapy must delay their attempt to conceive for at least six months.[4] Fertility preservation and pregnancy are to be discussed on an individualized basis depending on tumor pathology, cancer stages, and the patient's desire. Hence, we discuss a case of a 35-year-old, unmarried female patient with breast cancer where controlled ovarian stimulation, followed by oocyte cryopreservation, was done and analyze the psychological, social, ethical, and technical concerns.

Case Description

A 35-year-old woman, unmarried, diagnosed with nonmetastatic ductal carcinoma of invasive nature of the breast with positive for estrogen, progesterone and Her2 receptors, who was planned for neoadjuvant chemotherapy followed by conservative surgery and was referred to our *in vitro* fertilization (IVF) center for fertility preservation. She attained menarche at 14 years of age and had regular menstrual cycles with normal flow. She had no previous medical history, and her family history was not significant. Her body mass index (BMI) was 26 kg/m^2. Transvaginal ultrasound showed a normal-sized uterus with a normal cavity, ovaries with an antral follicle count (AFC) of 8, and anti-müllerian hormone (AMH) of 1.7 ng/mL. The patient underwent ovarian stimulation using the antagonist protocol from the second day of the menstrual cycle with recombinant gonadotrophin [recombinant follicle-stimulating hormone (rFSH)] in a dose of 200 IU subcutaneously and a daily dose of letrozole-5 mg was added. An average response was obtained, and on day 8, human menopausal gonadotropin 150 IU was added for 2 days. The response was optimum, and an injection of cetrorelix [gonadotropin hormone-releasing hormone (GnRH) antagonist] was added to oviate endogenous luteinizing hormone surge. On day 12 (when 4 follicles >16–18 mm), final oocyte maturation was done by giving a trigger with recombinant human chorionic gonadotropin 500 µg. Ovum pickup was done on day 14, and five oocytes were aspirated and cryopreserved.

Discussion

The patient was 35-year-old woman, unmarried, and opted for conservative surgery, referred for fertility preservation. After

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discussion, she agreed to oocyte cryopreservation. The consent process included a discussion on the effect of future infertility, treatment of cancer, option of fertility preservation, protocol of fertility preservation, realistic success risk, and cost of fertility preservation was discussed. The disposition of oocyte, embryo, ovarian tissue, and posthumous use of reproductive material are to be discussed with the patient. Alternative fertility options like donor oocyte programs, altruistic surrogacy, and adoption are to be debated.[5]

Oocyte cryopreservation is an efficacious and safe treatment for the eligible patient who desires fertility preservation. Due to advancements in oocyte vitrification techniques in assisted reproduction, the cohort of female in reproductive age choose to preserve their fertility for medical reasons or postpone childbearing.[6] Most important is that women should be properly counseled regarding the limitations and success of the technology.

The patient must consider the risk of radiotherapy and chemotherapy on future fertility before considering the treatment of preserving the fertility. During management of cancer breast, chemotherapy and hormonal therapy require at least two years for observation for complete remission.[7] Careful coordination with the oncologist team is required for fertility preservation for timely initiation of cancer treatment with the logical understanding that treatment takes precedence over fertility.

Before starting the chemotherapy, ovarian reserve is to be assessed with AFC, follicular stimulating hormone and AMH. This helps in the selection of gonadotropin doses and to anticipate the gonadotoxic effect.[8]

For ovarian stimulation GnRH antagonist protocol is preferred for oocyte and embryo cryopreservation. To prevent the risk of ovarian hyperstimulation syndrome, to induce oocyte maturation GnRH agonists are recommended in antagonist cycles.[7]

In estrogen-positive breast cancer, tumor cells are susceptible to the environment with estrogen excess.[8] Even though these tumors are classified as receptors negative, a certain minimal percentage of positive receptor cells are present.[9] Theoretically high levels of estrogen stimulate subclinical disseminated disease, but no clinical data is available, any drug that antagonizes the effect is reasonable.[10] For the management of micrometastatic disease, aromatase inhibitors have been found effective as adjuvant therapy.[11] Aromatase inhibitors such as letrozole act by inhibiting the aromatase enzyme which converts androgen into estrogen by process of aromatization and is used as ovulation induction drug and adjuncts in in controlled ovarian stimulation protocols.[12]

The success of the oocyte cryopreservation technique has improved because of vitrification. Vitrification solidifies the oocyte and surroundings directly in a glassy, vitrified glazed, shiny state, minimizing the formation of intra- and extracellular ice crystals. Meta-analysis supports the better survival after thawing and clinical outcomes achieved with oocyte vitrification.[13]

The optimal time duration between cancer diagnosis and starting of radiotherapy, chemotherapy, hormonal suppression, and attempting conception is important for fertility preservation.[14] When controlled ovarian stimulation is not possible or contraindicated, oocyte/embryo vitrification after oocytes are recovered from small antral follicles after *in vitro* maturation (IVM) can be discussed and attempted or ovarian tissue cryopreservation can be done.

A multicenter retrospective study on the role of elective fertility preservation (EFP) in improving the success of IVF cycles in individuals undergoing EFP before cancer treatment or decline in fertility due to age. The average number of oocytes aspirated and vitrified per cycle was lower in EPF for aging than in oncofertility patient (Onco-FP).[15] Only 12.1% women of the EFP group and 7.4% of the Onco-FP group returned to claim vitrified oocytes for further use. The generally survival rate of frozen oocyte was the same in both groups, but fewer EFP groups had embryo transfer. The aging of the women and likely increased proportion of chromosome aneuploid embryos are incompatible with further development. The cancer patients had lower implantation rate, because of underlying disease than in EFP patients. Maternal aging was the primary factor related to clinical success; 35 years is considered as the cut-off age. The young EPF women had improved results in terms of implantation, conception, and cumulative live birth rates than the same age of Onco-FP patients. The chance of cumulative pregnancy increased with the number of oocytes available for the thawing and fertilization. After 41 years of age, it did not show any benefit.[16]

Conclusion

The patient is to be counseled on fertility preservation options before starting chemo and radiotherapy for breast cancer. As per recent studies, young breast cancer patients with nonmetastatic disease have a better prognosis. Oocyte cryopreservation is efficacious and safe. In the past decade, including the option of IVF programs has been a great achievement. It is now a viable option for unmarried women who incline to preserve their oocyte for medical or non-medical purposes. According to current guidelines, it is recommended to defer pregnancy for two years. However, it is unlikely that conception within six months after diagnosis will decrease the chances of survival.

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