CASE REPORT

Fertility Preservation in Breast Carcinoma: The Way Forward

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Abstract

Fertility preservation is crucial to prevent the spread of cancer in younger adults, especially in women of reproductive age. A 30-year-old woman with breast cancer was referred for fertility preservation, despite having no family history of breast cancer. The couple was offered embryo cryopreservation before chemotherapy, and the procedure involved controlled ovarian stimulation (COS) with letrozole supplementation. The couple retrieved 13 oocytes, with 11 being metaphase 2 of which 9 fertilized. The oocytes were stimulated and monitored serially for blood estrogen levels. Fertility preservation is essential for improving the quality of life for cancer survivors and reducing concerns about increased estrogen levels in women with breast cancers. Multidisciplinary collaboration between oncologists and reproductive specialists is needed to improve awareness and availability. Early referral to a fertility specialist is essential for optimal results.

Keywords: Breast cancer, Case report, Fertility preservation, Infertility, Ovum pick up, Reproductive medicine.

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Introduction

In essence, fertility preservation refers to maintaining an individual's or couple is ability to start a family at any time. The incidence of cancer among young adults has been reported to increase. Breast cancer is one of the most prevalent malignant tumors among women of reproductive age in developed nations. Cases of 5–7% develop before the age of 40.[1]

Case Presentation

A 30-year-old woman married since 2 years, nulligravida, with right breast invasive carcinoma grade III, estrogen receptor positive, was referred for fertility preservation. She had no family history of breast carcinoma in the mother. Laboratory tests for complete blood count, sugars, thyroid, prolactin, liver and renal function tests, and INR were within normal limits. Antimullerian hormone level (AMH) was 3.4 ng/dL. On the second day of her menstrual cycle, her serum estradiol level was 21 pg/mL. Viral markers for both husband and wife were negative. Semen analysis had a volume of 2 mL, count of 15 million/mL, and motility (grade III + IV): 20% (15% + 5%), 58% abnormal sperms, and 2–3 pus cells. A transvaginal ultrasound showed an antral follicle count of 8 in both the ovaries. The couple was offered embryo cryopreservation prior to the start of chemotherapy. The stimulation and oocyte retrieval procedure, cost, risks involved, embryo freezing and thawing procedure, and survival and success rates were explained to the couple, and informed valid written consent for the same was obtained. The possible risks of rising sr. estradiol levels and consequent spread of malignant cells were also explained.

The method employed was controlled ovarian stimulation (COS) with letrozole supplementation. (COST-LESS). About 5 mg of letrozole once a day was started from the second day of menstrual cycle, followed by recombinant FSH 225 IU subcutaneous 48 hours later. Decision to oocyte retrieval time was 10 days, with 8 days of COS. Serial serum estradiol monitoring was done (Table 1).

We retrieved 13 oocytes, of which 11 were metaphase 2 oocytes, 9 fertilized, and 7 Day 3 grade A 8 celled embryos were formed, which were cryopreserved. The post oocyte retrieval, tablet, letrozole 5 mg was restarted once a day and continued for 10 days with serial estradiol level monitoring till serum estradiol levels were 43.04 pg/mL.

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Table 1: Day of letrozole stimulation and estrogen levels

Cycle monitoring and stimulation	*Serum estradiol levels*
Day 2 of menstrual cycle/ Day 1 of letrozole stimulation	21 pg/mL
Day 3 of gonadotropins/ Day 5 of letrozole stimulation	145.8 pg/mL
Day of trigger	
Day 8 of gonadotropins	319 pg/mL
Day 10 of letrozole stimulation	
Day 10 post oocyte retrieval	43.04 pg/mL

Discussion

Modern urban lifestyle has led to couples delaying childbearing to later years. So, when a breast cancer affects a young woman, it is often possible that she has yet to complete her family. The increased 5-year survival in breast carcinoma patients post chemotherapy and

radiotherapy has forged the need for fertility preservation. Cytotoxic chemotherapy and/or hormone therapy causes a decrease in the primordial follicle pool in a drug and dose related manner, which in turn accelerates decline in oocyte number and quality. Numerous fertility preservation methods are available for reproductive age women with breast cancer, including oocyte cryopreservation if unmarried and embryo cryopreservation if married. Oocyte maturation in a laboratory setting and preserving ovarian tissue through freezing are still undergoing experimentation in India. A correct choice of cryopreservation method and optimal timing for conception, determined by both the oncofertility specialist and breast oncologist, is essential for ensuring successful fertility preservation treatment.

Recent contact with chemotherapy drugs can lead to physical/genetic irregularities in collected eggs, and decreased ovarian reaction to treatment. Therefore, ovarian stimulation should not be done in a woman who has finished chemotherapy within the past 6 months.

During COS for *in vitro* fertilization (IVF), there is a worry that the serum E2 level could rise above normal, which may harm estrogen-dependent cancers like breast cancer. Letrozole is a medication that competes with the aromatase enzyme complex and is prescribed for patients with hormone receptor positive metastatic and non-metastatic breast cancer. It prevents the transformation of androgenic substrates into their estrogenic forms, leading to a reduction in estrogen levels within the ovary. This leads to the activation of the hypothalamic pituitary axis, resulting in an increase in gonadotropic secretion, leading to follicular growth. Letrozole enhances ovarian androgens, leading to stimulation of initial follicle development. When the diameter of the follicles exceeds 14 mm, it is associated with a serum E2 level of around 200 pg/mL Hence, by checking the serum E2 level on trigger day, it is possible to anticipate the amount of oocytes that will likely be collected.[2] According to Quinn et al., the use of letrozole may lead to a lower maturity rate (MII/total oocytes retrieved), even though the mature oocyte yield (MII/AFC) is similar to non-cancer patients.[3]

Stimulation can be started, (A) Conventionally—if the patient presents during her spontaneous menses, (B) When there is a window of 6–8 weeks between surgery and chemotherapy, (C) A random start protocol—with or without luteolysis achieved with gonadotropin-releasing hormone (GnRH) antagonist.[4] Post oocyte retrieval, tablet letrozole 5 mg once a day is reinitiated to prevent a rebound increase of serum estradiol levels. If the serum estradiol levels are more than 250 pg/mL monitoring is continued every three days till levels fall below 50 pg/mL. Pregnancy following chemotherapy is not considered unsafe, even in patients with a history of hormone receptor-positive disease (Fig. 1).

Protocol for a study using Letrozole supplementation in COS - COST-LESS. Letrozole, an aromatase inhibitor, is started two days

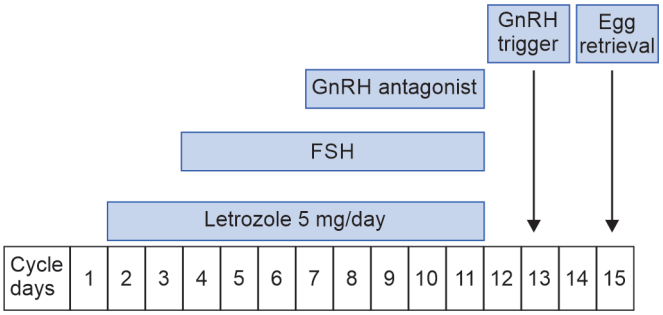

Fig. 1: Cost-less protocol

before beginning gonadotropin stimulation, on the second day of the menstrual cycle. Gonadotropin-releasing hormone antagonists are introduced once the dominant follicle grows to 13 mm to avoid ovulation before oocyte retrieval. In the present version of the procedure, a GnRH analog trigger (1 mg SC) is administered to start the oocyte maturation process, followed by oocyte retrieval 35 hours before ovulation occurs. The GnRH analog trigger helps suppress ovaries right after egg retrieval, aiding in reducing estrogen levels during the luteal phase.

Conclusion

Preserving fertility is increasingly crucial to enhancing the life quality of life for cancer survivors. The use of aromatase inhibitors may alleviate worries about elevated estrogen levels in women diagnosed with breast cancer. Collaboration between oncologists and reproductive specialists is necessary to enhance awareness and access. It is crucial to refer to a fertility specialist early in order to achieve optimal results.

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