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SHORT COMMUNICATION

Depot GnRH-agonist trigger for breast-cancer patient undergoing ovarian stimulation resulted in mature oocytes for cryopreservation: a case report


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Abstract This report describes the case of a 27-year-old woman with breast cancer who underwent ovarian stimulation for fertility preservation with recombinant FSH in conjunction with a gonadotrophin-releasing hormone (GnRH) antagonist and an aromatase inhibitor from the beginning of the treatment. A 3.75-mg triptorelin depot formulation was given intramuscularly when the follicular diameter of three follicles reached ≥ 20 mm and a total of 13 follicles reached ≥ 15 mm. Oocyte retrieval was scheduled for 36 h later and 10 mature oocytes were collected and vitrified. This case report demonstrates that a depot GnRH-agonist trigger effectively leads to mature oocyte retrieval, with the advantage of initiating ovarian suppression for the purpose of fertility preservation during adjuvant chemotherapy in breast-cancer patients. 

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Introduction

Given that premature ovarian failure is a frequent consequence of chemotherapy in young women with breast cancer and improvements in treating cancer have resulted in an increased number of long-term survivals, it has become of crucial importance to offer the patients efficient medical options of fertility preservation (Maltaris et al., 2008). Therefore, to improve the quality of life of breast-cancer

survivors, the issue of fertility preservation must be considered by any oncologist treating reproductive-age patients.

Options for fertility preservation include oocyte or embryo cryopreservation, ovarian protection by gonadotrophin-releasing hormone agonists (GnRH-a) and ovarian tissue cryopreservation (Blumenfeld, 2008; Donnez et al., 2008; Hulvat and Jeruss, 2009). To obtain mature oocytes for cryopreservation, patients must undergo ovarian stimulation. In this approach, final follicular maturation is more

frequently triggered by administration of human chorionic gonadotrophin but the use of GnRH-a has been proven to be an efficient method when hypophyseal blockage is performed with GnRH antagonists, with evident benefits regarding oestradiol concentrations (Oktay et al., 2010).

The purpose of this case report is to demonstrate that final follicular maturation may be achieved by administering a depot GnRH-a formulation. This approach would have the benefit of immediately initiating ovarian suppression for protection against chemotherapy gonadal toxicity.

Case report

A 27-year-old woman with breast cancer was referred to the Assisted Reproductive Unit of the Women's Health Reference Centre (Hospital Perola Byington, São Paulo, Brazil) for fertility preservation. The patient underwent left mastectomy and lymphadenectomy with immediate reconstruction. None of the dissected lymph nodes showed any evidence of metastasis and chemotherapy was scheduled to start in a couple of weeks.

The patient was first seen on day 7 of the menstrual cycle. An ultrasound scan was carried out, which showed normal ovaries and an endometrial thickness of 4 mm; no follicles >10 mm were observed. In order to obtain oocytes for cryopreservation, ovarian stimulation was immediately commenced with a daily subcutaneous injection of 200 IU recombinant FSH (Puregon; MSD, Brazil). GnRH antagonist ganirelix (0.25 mg/day, Orgalutran; MSD) and oral administration of anastrozole (2.0 mg/day, Arimidex; AstraZeneca, Brazil) were introduced concomitantly. A 3.75-mg triptorelin depot formulation (Gonapeptyl 3.75; Ferring, Brazil) was given intramuscularly when the follicular diameter of three follicles reached ≥ 20 mm and a total of 13 follicles reached ≥ 15 mm. Oocyte retrieval was scheduled 36 h later. Twelve oocytes were collected (one fractured zona and one immature) and 10 mature (metaphase II) oocytes were vitrified.

Discussion

Currently, fertility preservation in young patients undergoing cancer treatment is an issue of major importance as a result of the significant improvement of survival rates and life expectancy for this group of patients. The modern trend is to associate methods of fertility preservation, such as freezing ovarian tissue for transplantation after cancer therapy, ovarian stimulation for cryopreservation of oocytes and/or embryos and GnRH-a co-treatment during chemotherapy (Lee et al., 2006).

Although Oktay and Sönmezer (2008) stress that GnRH-a should not be offered as a proven method of ovarian protection, there is evidence that pharmacological ovarian suppression may be considered a useful co-treatment in chemotherapy (Blumenfeld, 2008; Blumenfeld and von Wolff, 2008). Recently, a prospective randomized trial showed that GnRH-a treatment reduces gonadotoxicity and is an effective method of fertility preservation (Badawy et al., 2009). Another recent prospective randomized trial found that the concomitant use of triptorelin with chemotherapy is associated with a significant increase in preservation of ovarian function in breast-cancer patients, when

compared with chemotherapy alone (Del Mastro et al., 2010).

With regard to ovarian stimulation protocols, hypophyseal blockage with a GnRH antagonist and the association of an aromatase inhibitor are effective alternatives in breast-cancer patients (Oktay et al., 2006). Co-administration of aromatase inhibitors in ovarian stimulation reduces oestradiol concentrations and may improve ovarian response by augmenting FSH receptor expression (Verpoest et al., 2006). Triggering ovulation with GnRH-a has been shown to be an efficient procedure when hypophyseal blockage is performed with antagonists, with the advantage of reducing oestradiol concentrations in comparison to triggering with human chorionic gonadotrophin (Oktay et al., 2010). Lower oestrogen exposure is a goal to be achieved in ovarian stimulation for breast-cancer patients. Reaching this objective would contribute to reduce concerns of oncologists and patients about ovarian stimulation safety. Moreover, randomized prospective studies support the notion that agonist-induced oocyte maturation completely eliminates ovarian hyperstimulation syndrome (Kol and Solt, 2008). As the suppressive effect of GnRH antagonists can be immediately reversed by the administration of GnRH-a (Fauser et al., 2002), there is no indication to discontinue GnRH antagonist on the day of the trigger. Ovulation trigger with GnRH-a is usually performed with subcutaneous administration of low doses of daily preparations, such as 0.5 mg buserelin (Humaidan et al., 2006), 0.2 mg triptorelin (Melo et al., 2009) or 1.5 mg leuprolide (Castillo et al., 2010).

The present case report demonstrates that the 3.75-mg triptorelin depot formulation efficiently promotes ovulation triggering due to the initial flare-up effect, allowing the retrieval of mature oocytes. This strategy has the advantages of, at the same time, inducing final oocyte maturation and initiating ovarian suppression for ovarian function protection against adverse effects of chemotherapy. As far as is known, this is the first report of the use of a GnRH-a depot formulation for ovulation triggering.

In conclusion, for the purpose of collecting oocytes for cryopreservation, the use of a depot GnRH-a formulation may be the method of choice for ovulation triggering in breast-cancer patients undergoing ovarian stimulation with GnRH antagonists, when ovarian suppression during chemotherapy is considered.

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