In-Vitro Fertilization: Donor Egg Sharing for Premature Ovarian Failure

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ABSTRACT

Premature ovarian failure may be a consequence of gonadotoxic cytotoxic chemotherapy or radiation therapy for malignant or systemic disease often resulting in major quality of life concerns. This is the first reported case in the English-speaking Caribbean using in-vitro fertilization (IVF) donor egg sharing in a patient who experienced premature ovarian failure following chemotherapy and radiation for Hodgkin's disease. The donor's indication was tubal factor infertility. Both patients delivered healthy infants.

Fertilización *In Vitro:* una Donante Comparte un Óvulo en un caso de Fallo Ovárico Prematuro

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RESUMEN

El fallo ovárico prematuro puede ser consecuencia de la quimioterapia citotóxica gonadotóxica o la terapia de radiación para alguna enfermedad maligna o sistémica, que a menudo trae consigo serios problemas para la calidad de vida. Se reporta el primer caso en el Caribe anglófono, en el que un óvulo de fertilización in vitro (FIV) de una donante, es compartido con una paciente que experimentó fallo ovárico prematuro tras ser sometida a quimioterapia y radiación a causa de la enfermedad de Hodgkin. El diagnóstico de la donante fue infertilidad por factor tubario. Ambos pacientes dieron a luz bebés saludables.

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INTRODUCTION

Hodgkin's lymphoma is a malignant neoplasm of lymphoid cells of uncertain origin. Worldwide, its peak incidence is in patients of the reproductive age group. In a ten-year review of Hodgkin's lymphoma in Jamaica, 69.2% of women were in the reproductive age group (1). The condition is generally treated by chemotherapy and/or radiotherapy. Chapman *et al* found that Hodgkin's patients with normal ovarian function who underwent therapy exhibited ovarian failure or decreased function in 49% and 34% of cases respectively; only 17% preserved normal ovarian function (2).

Donor IVF has been remarkably successful in providing children for women with premature ovarian failure, poor IVF responders and menopausal women (3). The method is four times more widely used in the United States of America (USA) where there is more consumerism, deregulation and the donors are paid, than in the United Kingdom (UK) and Spain (4). A single donor providing oocytes for multiple recipients has been reported from South America (5).

In-vitro fertilization has been available at the University of the West Indies, Mona Campus, Jamaica, since 2000 (6). Egg sharing in this case was carried out by adopting the code of practice as outlined by the regulatory body in the UK, the Human Fertilization and Embryology Authority (HFEA) (7). This is the first successful case of donor egg-sharing undertaken at this unit where an equal benefit-in-kind is afforded to both the donor and recipient.

CASE REPORT

This 38-year old para 0+3 woman presented in November 2006 expressing a desire to have children. Menarche was at age 12 years and she had regular menses up until the time of her treatment for Hodgkin's disease in 1992. Following chemotherapy and radiation, she became amenorrhoeic and remained so for 14 years. She was prescribed oestradiol valerate with ciproterone acetate that caused cyclical endometrial withdrawal bleeding.

In her obstetric history, she had 3 pregnancies that ended in first trimester losses in 1990 and 1998. She had no other medical history of significance. The physical examina-

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tion findings were within normal limits. Her investigations are listed in the Table. The patient's consort was age 50

Table: Blood test results for amenorrhoeic, recipient patient

FSH	72.3 IU/L (> 40 – menopause)
LH	23.4 IU/L (> 21– Menopause)
Oestradiol	< 73.0 pmol/L (73.0–184.0)
TSH	0.681 mIU/L (0.3–5.0)
T4	86.6 nmol/L (57.9–60.9)
Prolactin	201.0 mIU/L (0–434.0)
TVScan	Normal uterus with a 5 mm endometrial stripe

years and on treatment for hypertension. He did not have erectile dysfunction. He purportedly had 3 children the youngest being 17 years old.

In April 2007, she was scheduled for egg sharing with an anonymous donor. Prior to IVF, a 'mock' cycle of oestradiol valerate and progesterone was attempted to determine whether the endometrium would respond. It took 20 days for the endometrium to become 6.4 mm in double layer thickness.

The 31-year old para 0+1 donor, was diagnosed with tubal factor infertility. She was karyotyped (46XX) and matched for blood type with the recipient. All other serological and infection screening tests were normal. The donor undertook a long protocol ovarian hyperstimulation cycle. This comprised down-regulation with a gonadotropin-releasing hormone agonist, stimulation with purified human menopausal gonadotropin, serial transvaginal ultrasound monitoring and human chorionic gonadotropin (hCG) administration when a cohort of follicles attained a diameter exceeding 16 mm. Luteal support comprised progesterone pessaries and oestradiol valerate tablets.

Simultaneously, the recipient was stimulated with oestradiol valerate and then progesterone. The endometrial response this time was to 7.5 mm on Day 21, the day of embryo transfer.

The donor stimulated extremely well. Her Menopur™ dose was decreased on Day 7 from 225 to 150 units. On the day of hCG administration she had > 30 follicles with 14 measuring ≥ 14 mm. The oestradiol level was 3135 pg/ml. Twenty-eight eggs were retrieved by ultrasound guided needle aspiration employing conscious sedation with intravenous meperidine HCl and midazolam. The retrieved eggs were shared evenly between the donor and the recipient and were fertilized with sperm from their respective partners. The donor had 10 normally fertilized embryos of which two 8-cell embryos were transferred to her endometrial cavity; five of the remaining eight embryos were cryopreserved for possible later use. The recipient also had 10 normally fertilized embryos of which three (8-cells, 6-cells and 5-cells) were selected for transfer; the remaining embryos were not of adequate quality for cryopreservation. The embryos were transferred 48 hours after fertilization under ultrasound guidance.

At Day 14 post-transfer, both patients had a positive urine hCG pregnancy test. At Day 28 post-transfer, both patients had viable singleton gestations visualised on ultrasound. The donor did not develop clinical symptoms or signs of ovarian hyperstimulation syndrome.

In January 2008, the donor had a spontaneous vaginal delivery of a live female infant weighing 2.1kg with Apgar scores of 7 and 8 at 1 and 5 minutes, respectively. The following day, at another hospital, the recipient had a planned Caesarean delivery of a live female infant with Apgar scores of 9 and 9 and weighing 3.239 kg.

DISCUSSION

Both men and women with Hodgkin's disease are at risk of gonadal failure after standard chemotherapy regimens with no difference in the frequency and severity between the standard treatment schedules (8). In the past, these patients could only be counselled about adoption or face involuntary childlessness; IVF has however revolutionized the management of their infertility.

Several chemotherapeutic agents are potential gonadotoxins. Their use is central to the treatment of a variety of malignant and systemic diseases, often in individuals of reproductive age. A critical aspect of management for these patients must include referral for reproductive counselling prior to treatment.

Currently, the only widely available technology for women with ovarian failure, who want a pregnancy, is an IVF donor programme, as in this case. The pregnancy rates in donor programmes exceed 50% (9). Alternatively, patients may undergo ovarian super-ovulation for oocyte cryopreservation or IVF and embryo freezing, prior to chemotherapy, returning for frozen embryo transfer post-treatment. This is only applicable to patients with partners prior to treatment and excludes adolescents and children.

In contrast to cryopreservation of embryos and sperm, oocyte cryopreservation is more challenging since oocytes are more sensitive to cryoinjury. The meiotic spindle, cytoskeleton, cortical granules and zona pellucidae are the structures particularly at risk (10). Unfortunately, the results have been variable and not sufficiently successful for routine use (11). Ovarian tissue cryopreservation is available but only a few pregnancies have been reported; the first livebirth was in September 2004 (12). Due to the risk of ovarian metastases with different cancers, treatment must be individualized.

As cryopreservation technology becomes more advanced and widespread, the future management may be pretreatment cryopreservation of ovarian tissue for later re-implantation. This is currently practised in only a few centres worldwide. For this unit, continued investment in research and development will facilitate parity with these centres, thereby allowing better provision for the procreative liberty patients require and deserve.

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