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Case Report

Successful ongoing pregnancy following cryopreserved-thawed blastocyst transfer in an infertile Kallmann syndrome woman with balanced reciprocal translocation: a case report

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Summary

Kallmann syndrome (KS) is a genetic disorder characterized by hypogonadotropic hypogonadism, anosmia, and infertility, occurring in approximately one in 50,000 women. Here the authors present a unique case of successful ongoing pregnancy in an infertile KS woman with balanced reciprocal translocation [t(12;18)(q22;q21.1)]. The patient had a history of one sporadic miscarriage and low level of serum anti-Müllerian hormone, basal follicular stimulating hormone, luteinizing hormone, and estradiol concentration. She showed a good response to ovulation induction using human menopausal gonadotropin and chorionic gonadotropin and conceived in an in vitro fertilization and cryopreserved-thawed blastocyst transfer cycle.

Key words: Anti-Müllerian hormone; Balanced reciprocal translocation; Kallmann syndrome.

Introduction

Kallmann syndrome (KS) is a rare genetic disorder characterized by hypogonadotrophic hypogonadism and anosmia. KS affects both males and females with a clear male predominance (1 in 10,000 *vs.* 1 in 50,000). KS originates in mutations of several genes including *KAL1*, *FGFR1,* and *PROKR2,* which disrupt the migration of olfactory and gonadotropin releasing hormone-producing neurons in the fetal developing brain [1].

A number of successful pregnancy cases following ovulation induction have been documented in infertile KS women. Meanwhile, there are few reports on pregnancy in KS women complicated with chromosomal translocations, which potentially causes recurrent pregnancy loss. Here the authors present a unique case of successful ongoing pregnancy following in vitro fertilization (IVF) and cryopreserved-thawed blastocyst transfer in an infertile KS woman with balanced reciprocal translocation.

Case Report

A 32-year-old woman was referred to the present clinic for infertility treatment. Her menarche was at the age of 14, but her menstruation rarely occurred thereafter. She started to take low dose oral contraceptives when she was 24-years-old. After her marriage at the age of 27, she stopped medication to try to conceive, but had amenorrhea again. She consulted with a gynecologist seeking for infertility diagnosis. Her serum concentration of anti-Müllerian hormone (1.27 ng/ml), basal follicular stimulating hormone (FSH, 2.0 mIU/ml), luteinizing hormone (LH, < 0.1 mIU/ml), and estradiol (< 5.0 pg/ml) measured low. She showed a poor response to conventional ovulation induction, but had a pregnancy following one year of treatment, which resulted in miscarriage at eight weeks of gestation. She desired a chromosomal analysis, which identified balanced reciprocal translocation [t(12;18)(q22;q21.1)]. She failed to conceive in following infertility treatment including five IVF cycles.

When she presented to the present clinic, her body mass index was 19.7 (167 cm in height and 55 kg in weight). She did not own any specific physical feature, but a careful interview suggested the presence of her smell disturbance. Brain magnetic resonance revealed olfactory tract agenesis. Combined with low basal FSH and LH levels, she was diagnosed with KS. On cycle day 3, serum FSH was <1.0 mIU/ml, LH was < 0.2 mIU/ml, estradiol was 26.4 pg/ml, and antral follicle count on transvaginal ultrasound was 5. On cycle day 9, serum FSH (2.3 mIU/ml), LH (< 0.2 mIU/ml), and estradiol (< 20 pg/ml) remained low. As the couple desired IVF treatment, daily human menopausal gonadotropin (hMG) injection (300 IU/day) was initiated. On cycle day 17, the total follicle count increased to 18 with a 20-mm leading follicle, FSH 30 mIU/ml, LH < 0.2 mIU/ml, and E2 984.1 pg/ml. Transvaginal ultrasound-guided oocyte pick up was performed 36 hours following 10,000 IU human chorionic gonadotropin (hCG) administration. The total dose of hMG during controlled ovarian stimulation was 3,600 IU. Thirteen oocytes were retrieved and inseminated (seven oocytes for conventional IVF and six for intracytoplasmic sperm injection). On days 5 and 6, a total of five blastocysts were cryopreserved. One of frozen blastocysts were thawed and transferred in the subsequent hormone replacement cycle using conjugated estrogens and progestogens. Blood examination showed positive serum hCG (230.4 mIU/ml) after 11 days of the embryo transfer. Her healthy intrauterine singleton preg-

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nancy is ongoing at 16 weeks of gestation.

Discussion

There are a few articles in the literature on male KS patients with balanced reciprocal translocations [2, 3]. To the best of the present authors' knowledge, this is the first case of KS women with balanced reciprocal translocation. The relationship between [t(12;18)(q22;q21.1)] and KS/infertility remains unknown. One of the genes localized to 12q22 is *LGR5*, of which conditional deletion in mouse female reproductive organs causes insufficient ovarian progesterone secretion and subfertility [4]. *SMAD7* is a gene located in 18q21.1 and involved in transforming growth factor-β signaling which plays a crucial role in the increase and growth of neurites, as well as neural migration and axon outgrowth and guidance [5]. The prevalence of chromosomal abnormalities has been estimated to be 6-10% in couples with recurrent pregnancy loss [6]. In the present case, the patient had a history of sporadic miscarriage in the first trimester, but current pregnancy is uncompromised so far.

KS women generally have both low anti-Müllerian hormone levels and antral follicle counts, but their decrease can be reversed by administration of hMG agents [1]. The present patient also had a low serum anti-Müllerian hormone concentration for her age, but showed a good response to ovulation induction using a combination of hMG and hCG and conceived in an IVF and cryopreserved-thawed blastocyst transfer cycle.

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