PARTIAL HYDATIDIFORM MOLE FOLLOWING TRANSFER OF FROZEN EMBRYOS FROM ICSI CYCLES -2 CASE REPORTS

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ABSTRACT

Objective : Hydatidiform mole is the most common gestational trophoblastic disease. The partial hydatidiform mole (PHM) is typically triploid with one maternal and two paternal haploid numbers. In intacytoplasmic sperm injection (ICSI), only one sperm is injected, thus the formation of triploid embryo would result from either injection of an abnormal sperm which contains the diploid number or replication of the haploid sperm inside the oocytes after the injection. Diploidy is the most common chromosomal anomaly in the sperm of patients with oligozoospermia. Thus, male factor infertility can predispose to such abnormal outcome. Two cases of partial mole following the transfer of frozen embryos from ICSI cycles are discussed in this report.

Key words : Partial hydatidiform mole, ICSI, Frozen Embryo Transfer

INTRODUCTION

Intracytoplasmic sperm injection (ICSI) can be used for men with severely defective semen profiles: obstructive azoospermia (OA), non-obstructive azoospermia (NOA), and oligoasthenoteratospermia (OAT). The ICSI procedure allows for the direct injection of a single sperm into the cytoplasm of the oocyte, and fertilization is possible in instances of previous failed fertilization after IVF treatment.

Hydatidiform mole is the most common gestational trophoblastic neoplasm with higher incidence in the Far East compared to the Western countries. A partial mole contains the triploid number of chromosomes, two sets of which are paternal in origin occurring through different mechanisms.

ICSI involves the injection of a single sperm into the oocyte to complete the diploid number of chromosomes and as such should minimize the incidence of triploid PHM. However, injecting a diploid sperm or the replication of a haploid sperm after injection cannot be prevented. Here are two case reports of PHM that occurred after transfer of thawed embryos resulting from ICSI cycles for the treatment of severe male factor infertility.

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CASE REORT 1

A 34 years old woman was being treated for infertility for 5 years due to severe male factor infertility. Semen analysis showed severe OAT with a volume of 0,8 ml, count $7x10^6$ / ml, motility 30% and abnormal forms 70% Day 3 FSH and Oestradiol levels were normal as was a tubal patency test. A previous ICSI cycle with fresh embryo transfer resulted in a live birth. In the subsequent treatment , ovulation induction resulted in 28 eggs, all of which were injected but only 19 fertilized. In view of the risk of Ovarian Hyperstimulation syndrome (OHSS), all fertilized oocytes were frozen at the pronuclear stage.

A few months later, 5 embryos were thawed resulting in 5 live embryos with subsequent transfer of two embryos that resulted in a clinical pregnncy. Unfortunately, this ended as a missed miscarriage and evacuation of the uterus at 10 weeks gestation. No molar tissue was seen at histo-pathological examination.

In another frozen embryo transfer (FET) cycle 5 embryos were thawed. Thawed embryos were incubated overnight i.e. 20-24 hours allowing cleavage to occur. Two embryos were replaced (grade 2B & 2C) and this resulted in a clinicl pregnancy. A positive pregnancy test occurred 14 days after embryo transfer. Ultrasound scanning at 7 weeks showed a fetal pole but no fetal heart pulsations were observed. Diagnosis of missed miscarriage was made at 8 weeks and evacuation of the uterus was carried out. Histopathology showed small villi with hydropic changes with excessive multipolar proliferation of trophoblast and extra-villous trophoblastic proliferation. This histopathology was reviewed in the Trophoblastic Tumour Screening and Treatment Center in Charing Cross Hospital and partial hydatidiform mole was diagnosed. The patient was registered with Charing Cross Hospital for follow up.

CASE REPORT 2

A 29 years old woman had a 2-year history of infertility associated with significant male factor problems. Semen analysis showed severe OAT with a volume of 1.8 ml, count 10 x 10^6 / ml, motility 5% and abnormal forms 75%. All female investigations were normal. Ovulation induction resulted in retrieval of 49 eggs, all of which were injected but only 17 fertilized. In view of the risk of OHSS, all fertilized oocytes were frozen at the pronuclear stage.

Two cycles of FET did not result in clinical pregnancy. In her third FET, 6 embryos were thawed and 5 survived. Two embryos were replaced 24 hours after thawing at the cleavage stage and this resulted in a clinical pregnancy. Pregnancy test was positive after 14 days. On ultrasound scanning at 7 weeks, a fetal pole with fetal heart pulsations was seen. Due to per vaginal bleeding, rescan at 9 weeks diagnosed missed miscarriage and the woman underwent suction evacuation of the uterus. As in the previous case, histopathology at the same hospitals diagnosed molar pregnancy with subsequent follow up at Charing Cross Hospital.

DISCUSSION

Triploid PHM may either arise through fertilization of a haploid oocyte by one spermatozoon that doubles its chromosomes after fertilization, or two sperms (one maternal and two paternal contributions) or fertilization with a sperm that contains the diploid number of chromosomes [1]. Another rare mechanism is the fertilization of a diploid oocyte from the fusion of two ova ("dieggy") by a haploid sperm [2].

Bernardini et al., 2005 showed that infertile men

with total normal motile count < 2 x 10^6 were found to be at increased risk for sperm aneuploidy and diploidy[3]. Rubio et al., (2001) also found that semen samples of men with oligoasthenoteratospermia (OAT) were associated with significant increases in sex chromosome disomies, disomy for chromosomes 18 and 21, and the percentage of diploid sperm, particularly in those samples with markedly reduced sperm concentration (<5 x 10^6 / ml spermatozoa) [4].

Rubio et al., (2001) also found that the mean diploidy rate in their series of semen samples with OAT was 0.28%, reaching 0.45% in the subgroup of patients with counts of <5 x 10^6 / ml, both being significantly higher than that observed in the group of normozoospermic patients (0.10%)[4]. Egozcue et al., (2002) in their analysis of male pronuclei in 3PN zygotes produced by ICSI with sperm from oligo-, crypto- and azoospermic males revealed that 33.3% of them were diploid[5]. They also concluded that most diandric triploids produced by normo- zoospermic males by dispermy, while most diandric triploids produced by oligozoospermic males would result from fertilization by unreduced, diploid sperm[5].

Pfeiffer et al., (1999) showed significantly higher diploidy and total aneuploidy rates in ten OAT patients undergoing 11 ICSI cycles. Overall fertilization rate was 70%, but only two successful pregnancies were achieved. In addition[6], Vendrell et al., (1999) demonstrated that sperm concentration of <5 x 10^6 / ml was a predictor of meiotic abnormalities [7].

It may be logic to conclude from the above evidences that sperm diploidy can play a significant role in the formation of the triploid PHM especially in men with severe male factor infertility. Some has shown that the use fluorescence in situ hybridisation (FISH) to analyse the decondensed sperm heads allows the study of chromosomal abnormalities in men with OAT and may be important before proceeding with ICSI procedure [8].

Kowalik e t al., (1998) on their study on three hundred and thirty eight cryopreservation cycles, during which 1471 embryos were cryopreserved found that ICSI does not have an adverse impact on the survival and successful implantation rates of cryopreserved and thawed embryos[9]. So, cryopreservation itself would not be responsible for the abnormal outcome that is likely to happen either shortly after the injection or with resumption of division after embryo thawing.

Ulug et al., (2004) in their similar case report of PHM following the transfer of single frozen-thawed embryo subsequent to ICSI stated that checking for dipronuclear fertilization should markedly reduce the possibility of transferring a triploid embryo [10]. However, triploidy arising from diploid spermatozoa is not usually apparent at the pronuclear stage.

A number of case reports now reported the occurrence of partial or complete hydatidiform moles after assisted reproductive treatment. The two cases described here occurred in close succession, both in cases of severe male factor infertility. Careful check of fertilization and the number of pronuclei is of paramount importance. The possibility of that outcome may be mentioned to the patients especially those having their treatment due to male factor infertility.

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