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Case Report

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Counselling Considerations for Chromosomal Mosaicism after Embryo Biopsy PGT-A: A Case Report

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Abstract

Pre-implantation genetic testing for aneuploidy PGT-A is a genetic test performed on Day 5 or Day 6 embryos obtained through Invitro fertilization (IVF). Embryo Biopsy is a procedure where the part of Trophoectoderm of the embryo is taken and sent for PGT-A analysis. PGT-A is indicated in couple who has been through previous miscarriage, maternal age >35 years and previous child anomalies. Mosaicism is a condition in which the presence of two or more abnormal cell lines or a normal and an abnormal cell line has observed. Embryonic mosaicism might play a significant role in pregnancy loss after IVF, cytogenetic and array based analysis of miscarriages following spontaneously conceived pregnancies commonly reveal chromosomal mosaicism. The degree of Embryonic Mosaicism negatively affects the implantation rate.

Keywords: PGT-A; Genetic Counselling; Embryo Biopsy; Aneuploidy.

INTRODUCTION

Pre-implantation genetic testing for aneuploidy PGT-A is a genetic test performed on Day 5 or Day 6 embryos obtained through In vitro fertilization (IVF). Embryo Biopsy is a procedure where the part of the trophoectoderm of the embryo is taken and sent for PGT-A analysis. PGT-A is indicated in a couple who has been through a previous miscarriage, maternal age >35 years, and previous child anomalies.[1,2]

Chromosomal Mosaicism is a condition of an embryo that contains a normal cell line and an abnormal cell line. Chromosomal Mosaicism is a condition more often due to the non-disjunction of chromosomes post-zygomatically which leads to a monosomic line and a trisomic line. Chromosomal Mosaicism of each chromosome has been reported with a wide variety of morphological defects. However, some studies showed that chromosomal mosaicism may not affect the further development as there might be auto correction of the embryo genetics.[3,4]

CASE PRESENTATION

Based on the case study, we have observed a

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couple in which a female patient of age 36 and a male patient of age 43 years have participated in an IVF cycle. The patient has previously undergone 2 IVF cycles which have failed and after approaching us for 3rd cycle, they were interested to undergo PGT–A Analysis. As per the Antagonist protocol, the ovarian stimulation was performed and the ovum pick up (OPU) was conducted at the 34th hour after triggering with HCG. A total of 10 follicles were obtained and subjected to Intra Cytoplasmic Sperm Injection (ICSI) where the male patient's sperm count was observed as 55 million/mL and progressive motility as 40%. On day 5, five full blastocysts were formed and the trophoectoderm biopsy was performed for all the samples and sent to the laboratory for Comparative Genomic Hybridization (CGH).

PGT-A Analysis Report of Five Embryos (ECR/1301/Inst/TG/2019)

ID	QC	Results (CGH)
E1	PASS	Segmental loss of 5mb and 8mb has been observed in chromosome 11 & 18 Multiple mosaic gain and loss (more than 30mb) has been observed.
E2	PASS	Segmental loss of 2-10mb has been observed in chromosome 17 & 20
E3	PASS	Multiple aneuploidy has been observed
E4	PASS	Mosaic loss of 109mb has been observed in chromosome 1
E5	PASS	3mb loss of chromosome 9 & 19

Based on the following laboratory report, both patients were counseled about the aneuploidy, segmental loss, and Mosaicism of Embryos. After 2 months, the frozen embryos such as E1, E2, and E5 were thawed and were transferred to the female patient. The pregnancy test was conducted after 14 days of embryo transfer and it showed a positive result. The ultrasound scanning was performed after 6 weeks and it was observed by imaging to have a single fetal sac and after 9 months the female patient delivered a healthy baby.

Counselling Considerations for PGT-A

As per the protocol before going for the PGT-A, these guidelines were followed accordingly such as:

Pre-test genetic counselling: The patient before going for the PGT–A Analysis has to be informed about the risks, benefits and limitations while undergoing with this technology.[3]

Post-test genetic counselling: In this method, the euploid embryos has to be the first option for transferring as well as the degree of mosaicism, segmental loss or gain of embryos has to be analyzed. The embryo which is having the least aneuploidy embryo has to be selected for this transfer. Based on the laboratory results and conditions, the embryos whose genetic analysis is correlating with any known syndrome has to be reported or informed to the patient as well as with concern cautiously it has to be advised to the patient not to go for the transfer.[3,4,5]

Pre-natal Testing: Before going for the pre-natal testing, the couple has to be provided with a counselling to explain about the constraints and advantages of prenatal screening. Chorionic villi sampling (CVS) is of placental origin which offers the initial prenatal diagnosis for aneuploidy. Amniocentesis represents more of fetal tissues embryonic ectoderm and amnion Amniocentesis is more accurate, however normal amniocentesis does not interpret low level of mosaicism.[3,4]

DISCUSSION

As per the observations and growth of embryos, E1, E2, and E5 have been chosen for embryo transfer. It has been observed from the genetic analysis that Embryo E1 has a Segmental loss of 5 mb and 8 mb which is observed in chromosome 11 & 18 and multiple mosaic gain and loss of more than 30 mb has been observed. In this same manner, embryo E2 has a Segmental loss of 2-10 mb in chromosomes 17 & 20, and embryo E5 has a 3 mb loss of chromosomes in 9 & 19. Due to the multiple aneuploidy nature, the embryo E3 has not been chosen and also E4 has been not chosen in the same cycle transfer due to the presence of mosaic loss of 109 mb in chromosome.[1]

An abnormal cell line. The percentage of mosaicism may or may not correlate with the mosaicism of the embryo as the test is done by trophoectoderm biopsy which forms the placenta of the embryo. Mosaicism is a condition more often due to the non-disjunction of chromosomes post-zygomatically which leads to a monosomic line and a trisomic line. Mosaicism of each chromosome has been reported with a wide variety of morphological

defects. Patients have to be counseled for the most common syndrome with mosaic embryos which includes down syndrome, syndromes including x and y, 13 and 18 trisomy, Syndromes including Intra Uterine Growth Retardation, and Uni Parental Disomy. However, some of the Mosaic aneuploid Embryos might show Auto correction on further division and might become a normal embryo.[7,8]

CONCLUSION

PGT-A is a pre-implantation genetic screening for aneuploidy and it is a procedure that is recommended in Advanced Maternal age, Previous Miscarriages, and Previous child anomalies. Mosaicism is a common phenomenon that is observed in most Embryo biopsy cases. The patient should be counseled properly before going to PGT-A and informed regarding the risk of having an abnormal baby after Embryo transfer. In our case, a Healthy baby was born, even though, the transferred embryos has Mosaicism and segmental loss/gain.[3]

PGT-A Embryos which are reported with chromosomal mosaicism have to be dealt with carefully. Patients should be informed regarding the risks of chromosomal mosaicism. Patients have to be counseled for the most common syndrome with mosaic embryos which includes Down syndrome, syndromes including x and y, 13 and 18 trisomy, Syndromes including Intra Uterine Growth Retardation and Uni Parental Disomy, and counsel them not to go for embryo transfer in such cases. Patients after PGT-A have to go under Amniocentesis for further evaluation of the fetus and if any abnormality is reported has to for medical termination of pregnancy (MTP).

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