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Case Report

Transfer or not to transfer? a medical dilemma

Neeta Singh, Garima Patel*, Monika Saini, Ankita Sethi

Department of Obstetrics and Gynecology, AIIMS, New Delhi, India

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***Correspondence:**
Dr. Garima Patel,
E-mail: minnie.patel2@gmail.com

ABSTRACT

Morphological assessment predominantly determines the quality of embryos although, several methods are available for it. Dilemma to transfer arises when clinicians are left with mere poor grade embryos. This case report encompasses a case of 37 years primary infertile female managed with GnRH antagonist cycle for tubal factor infertility. Post ovarian stimulation and ovum pickup, only two 4 celled grade-C embryos were available for transfer. Reluctantly the embryo was transferred, but fortunately resulted in a healthy live intrauterine pregnancy. This case report questions the aptness of the current methods to determine embryo quality and also enlightens whether the ethical or medical conundrum holds true regarding relation between embryo quality and chances of a fruitful pregnancy.

Keywords: Poor grade embryo, Embryo transfer, Pregnancy outcome

INTRODUCTION

Embryo quality is the essence of an assisted reproductive technique (ART) cycle. All the efforts are aimed at achieving highest quality embryos. Selection of embryos for transfer constitutes an important component of in vitro fertilization (IVF) treatment. The embryos can be graded by various methods of morphological grading, but Istanbul consensus is most commonly accepted criteria.[1,2] In order to maximize the clinical outcomes following an IVF cycle, the novel time lapse microscopy (TLM) technique has been developed to aid the conventional morphological assessment method.[3] The morphological assessment is a key predictor of both implantation as well as clinical pregnancy rate in IVF cycles.[4,5] Current literature regarding morphological assessment and guide to embryo selection is immense. But as clinicians, the dilemma to transfer the only available poor grade embryos is encountered frequently in day-to-day clinical practice with no definite consensus.

This case report brings forth one such similar case wherein successful pregnancy is achieved despite transfer of the only two available 4 celled grade-C embryos.

CASE REPORT

Patient X, a 37-year-old woman presented with primary infertility for 10 years. After detailed clinical evaluation, examination and investigations, she was diagnosed with tubal factor infertility. The hormone profile comprised: FSH-6.33 IU/ml, LH -5.7 IU/ml, PRL-23.63 ng/ml and AMH-2.5 ng/ml. Her husband was found normal following semen analysis. Hysteroscopy done prior to IVF revealed normal cavity size, shape, bilateral ostia visualised clearly. At recruitment, the initial total antral follicle cohort was 6-7. Patient underwent GnRH antagonist cycle according to the aforementioned stimulation protocol (Table 1).

Six oocytes were finally formed and retrieved after 36 hours of dual trigger (Inj. Recombinant HCG 250 ug with Inj. Leuprolide 1 mg subcutaneously). Among the six oocytes, they were equally distributed into grade 1 and 2. Conventional IVF was done resulting in 4 fertilised embryos and they attained cleavage stage of embryo development on day 2. But due to poor ovarian response and poor grade (4 celled grade C) embryos, it was a dilemma whether to transfer or not to transfer the poor-quality embryos. But finally, the decision was taken to

transfer the only available day 2 embryos. Urine pregnancy test and beta HCG was done after 16 days and fortunately it was positive. Single live intrauterine fetus was documented at 6 weeks ultrasound scan and luteal phase support (Vaginal micronized progesterone 400 mg BD and injection micronized progesterone 100 mg intramuscularly OD) continued throughout 1st trimester. The first trimester screening and level II USG is negative for any chromosomal aneuploidy and gross congenital anomalies, suggesting healthy ongoing pregnancy.

Table 1: Stimulation protocol used for the patient.

Day of stimulation	1	2	3	4	5	6	7	8	9
Inj. FSH dose (IU)	300	300	300	300	300	350	350	350	300
Inj. HMG (IU)	75	75	75	75	75	75	75	75	-
Inj. Cetrorelix (mg)	-	-	-	-	-	0.25	0.25	0.25	0.25

DISCUSSION

On morphological assessment, the poor-quality embryos are generally not transferred during ART cycle and is either discarded or used for research/teaching purposes.[6-8] But the question arises whether this assessment technique aptly predicts the reproductive potential of the embryo. Kirillova et al demonstrated a lower implantation rate with poor quality day 3/5 embryo but those which implanted successfully possess similar potential to result in live birth comparable to fair or good quality embryos, thus supporting their transfer in dire circumstances.[9]

The concern arises regarding the inferiority of day 2 embryo transfer (ET) compared to day 3 embryos. This necessitates the need to prognosticate the patient prior to day 2 embryo transfer. Various studies report higher pregnancy and implantation rates with day 3 ET compared to day 2 ET.[10,11] But Lee et al in a prospective study concluded equivalent clinical pregnancy, ongoing pregnancy, abortion, and implantation rates per cycle between day 2 and 3 ET. Thus, suggesting non-inferiority of day 2 ET than day 3 ET.[12]

Another concern while transferring such poor-quality embryo is increased probability of chromosomal abnormalities in foetus.[13] Although various studies have established that morphological assessment does not correlate with ploidy status of the embryo but the mere consequence of such mishaps forces the IVF specialists to forgo evidence-based practice and falls prey to the common sense.[14,15] However this risk can be predetermined with preimplantation genetic testing (PGT) but it is an invasive procedure.[16] Also, employment of PGT does not translate to improved ongoing pregnancy rate.[17,18] Although blastomere biopsy is more reliable but it is associated with a dramatic 39% relative reduction in implantation rate of biopsied embryos compared to unbiopsied embryos.[19] Chromosomal mosaicism is highest at day 2/3 stage of preimplantation embryo development and building on this, a two-blastomere biopsy strategy has been proposed.[20] However, this might involve a depletion of up to 25% of the embryonic mass and in turn impact clinical outcomes.[21] However, ESHRE 2010 guidelines suggested that this procedure can be safely employed when embryos are composed of ≥6 cells with less than 30% of fragmentation.[22] With fear to lose the only available two embryos, PGT was not done for the current patient as advanced age and poor ovarian reserve precluded her only reasonable chance to conceive with her own oocyte. These limitations can be overcome by time lapse imaging which aids in differentiating between euploid and aneuploid embryos, however poor accuracy prohibited its' employment to replace preimplantation genetic testing for testing aneuploidy.[3]

As mentioned in case description, the ongoing pregnancy did not show any evidence of chromosomal aneuploidy and gross congenital anomaly. In tandem to our experience, similar favourable results are reported in a large case-control study by Mendoza et al demonstrating no increased risk of congenital malformations and perinatal complications despite transferring very poor-quality embryos.[13]

CONCLUSION

This case report highlights the probability of all viable embryos to implant irrespective of their morphological grading. When heralded with such dilemma, embryo transfer can be safely done to explore even the slightest opportunity of positive outcome after appropriate patient counselling. This report also highlights the poor correlation between the current morphological grading system and chances of successful pregnancy warranting the need to explore more reliable predictors.

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