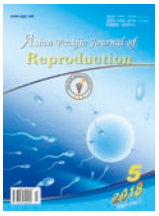

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Monozygotic twinning after donor egg intracytoplasmic sperm injection-A case report

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ABSTRACT

We are reporting a case of monozygotic twinning after donor egg intracytoplasmic sperm injection (ICSI). A 34-year-old lady presented to our centre with primary infertility due to severe endometriosis and low egg reserve. ICSI with donor eggs was planned. A 24 years old voluntary oocyte donor was investigated and stimulated under antagonist protocol. Total 21 eggs and all in metaphase Ⅱ were retrieved. These eggs were injected with the patient's husband sperms by ICSI. Patient's endometrial lining was prepared under hormonal replacement therapy protocol. Two expanded blastocysts were transferred on day 5 of progesterone. Beta human chorionic gonadotropin was positive after 10 days. The first antenatal scan at 6 weeks could pick up only two sacs indicating twin conception. Repeat scan at 12 weeks revealed tri-amniotic triplet conception with two foetuses sharing the same placenta (triamniotic pregnancy with monochorionic twins). The patient was counselled about risks associated with triplet conception and was advised of embryo reduction. Two mono chorionic twins were reduced under ultrasonography guidance. Single pregnancy continued till 21 weeks after which the patient miscarried spontaneously. It is difficult to identify the subset of patients at risk for monozygotic twinning; hence, all patients should be counselled about possibility of monozygotic twinning while deciding the number of embryos to be transferred.

1. Introduction

While multiple pregnancies due to dizygotic twinning after intracytoplasmic sperm injection (ICSI) are not rare, the same is not true for monozygotic twinning. Monozygotic twinning occurs when a single zygote divides into two embryos. Reported incidence of monozygotic twins is 0.40%-0.45% in general population[1] and is 1.10%-1.20% in assisted reproduction technology (ART)[2,3].

Placentation and chorionicity depends on the stage of embryo at the time of division. It can be assessed by ultrasonography markers like lambada sign[4], though the finite diagnosis is only possible through DNA profiling. Here, a case of monozygotic twinning after donor egg ICSI is presented.

2. Case history

A 34 years old patient presented to our centre with primary infertility. She had undergone laparoscopy for severe endometriosis. Her anti-mullerian hormone was 0.5 ng/mL. Her husband's semen parameters were in normal range. She was planned for ICSI with donor eggs in view of severe endometriosis and low egg reserve.

A 24 years old voluntary oocyte donor with a body mass index of 24.03 was recruited for her after investigations. Donor's menstrual cycles were regular and she had one child borne through natural conception. Her investigations including hormonal parameters and karyotype were normal. The antral follicle counts were 15.

She had donated three times previously at our centre. In the first case the outcome was negative after transfer of two blastocysts in a frozen transfer. In the second cycle, two fresh blastocysts were transferred which resulted in a single pregnancy. In the third cycle, two blastocysts were transferred in a frozen transfer. The beta human chorionic gonadotropin was positive, the first antenatal scan showed twin live conception at 6 weeks. On subsequent scans, only single pregnancy continued.

This was the fourth cycle for her. She was stimulated with human menopause gonadotropin in standard dosage under antagonist protocol from the second day of her cycle. Ovulation was triggered with gonadotropin-releasing hormone agonist (*inj.* decapeptyl 0.2 mg subcutaneously) when at least 3 follicles reached 17 mm. The ovum pick up was scheduled between 34 to 35 h after the trigger. Total 21 eggs were retrieved; all of them were in metaphase Ⅱ . The eggs were injected using the husband's sperms. The embryos were cultured in sequential media till day 6.

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Meanwhile, the patient's endometrium was grown with estradiol valerate 8 mg from the second day of cycle. Progesterone was added from day 9 of her cycle, on the day of egg retrieval of voluntary oocyte donor, when the patient's endometrium reached 10 mm (trilaminar). Two expanded blastocysts were transferred in fresh cycle on day 5 of progesterone. Six blastocysts were frozen on day 6.

The beta human chorionic gonadotropin 10 days after the embryo transfer was positive. The patient was referred to obstetrician for antenatal care. The first antenatal scan was done with her obstetrician, and it showed 6 weeks dichorionic twin conception. Subsequent scan was done at 12 weeks at a higher centre, and it showed triamniotic pregnancy with two foetuses sharing the same placenta (triamniotic pregnancy with monochorionic twins). The patient was counselled about risks associated with triplet conception and referred for embryo reduction. Under ultrasound guidance two monochorionic twins were reduced and single pregnancy continued till 21 weeks. The patient miscarried spontaneously at 21 weeks.

3. Discussion

Incidence of monozygotic twinning was found to be more in ART than natural conception. It is stated to be varying from 1.1%-1.2%[2,3]. Various authors have tried to ascertain the etiopathogenesis and risk factors associated with it.

ICSI though initially proposed as a risk factor is found to have no significant association with monozygotic twinning[5]. The incidence is found to be more in fresh embryo transfers than frozen ones[3].

Monozygotic twinning is observed more often in blastocyst transfers than cleavage stage transfers by various authors[2,6,7]. Particularly, transfer of an advanced stage blastocyst was found to be more associated with this phenomenon[8]. In contradiction to this finding, Franasiak *et al* have reported that blastocyst transfer is not associated with increased incidence of monozygotic twinning after controlling embryo cohort quality[9]. In our case the embryo transfer was a fresh embryo transfer of blastocysts after donor egg ICSI.

According to Sobek *et al*, Monozygotic twinning after ART is related to genetic factors rather than ART technique itself[10]. Neither the patient nor the voluntary oocyte donor in our case had previous twin conception, but we have not noted a thorough family history of twinning up to the third generation as the authors recommend.

The same voluntary oocyte donor in previous three cycles of egg donation has given once single pregnancy and once dizygotic twins; but never monozygotic twins. Considering this background, the genetic association in our case seems like a distant possibility. Assisted hatching was also proposed as a risk factor for monozygotic twinning[7]. The embryos in our case were not exposed to assisted hatching.

Sometimes a natural conception occurring simultaneously can give rise to more number of gestational sacs on ultrasonography than the number of embryos transferred[11]. In such a scenario, the pregnancy should be trichorionic as it is developing from three zygotes. In our case, the patient was monitored from the second day of her cycle and it was observed that her follicle didn't grow naturally. The endogenous serum progesterone before starting her on vaginal micronized progesterone was 0.27 ng/mL. The chorionicity as assessed on ultrasound suggests triamniotic triplets with monochorionic twins. All these did not support the possibility of a concurrent natural conception.

The exact mechanism which is responsible for splitting of the zygote in our case seems elusive. Larger studies are needed to understand the mechanism of monozygotic twinning, so that precautions can be taken to avoid it. This is particularly important in today's era as the world is moving towards more and more single embryo transfers in an attempt to have a single and healthy pregnancy.

In conclusion, it is difficult to identify the subset of patients at risk for monozygotic twinning. The possibility of monozygotic twinning should always be kept in mind when we decide about how many embryos to be transferred and the patients should be properly counselled about it before the procedure.

Conflict of interest statement

We do not have any conflict of interest here.

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