Dizygotic Triplet Pregnancy with Monoamniotic Twin Component Occurring After Intracytoplasmic Sperm Injection: A Case Report

Ismet Gun, Nafi Sakar, Ali Ruştü Ergur

GATA Haydarpşa Training Hospital, Department of Obstetrics and Gynecology, Istanbul, Turkey

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Abstract: The etiology of dizygotic triplet pregnancy with monozygotic twin component is unknown but the role of assisted reproductive techniques in monozygotic multifetal pregnancy is unclear. Zonal manipulation could be an important factor in increasing incidence of monozigotic twin pregnancy. In addition, the possibility of monozygotic twinning after assisted reproductive techniques is higher than in the general population. In this report, we present a case of dizygotic triplet pregnancy with monoamniotic twin component after assisted reproductive techniques. Further similar studies are needed to understand the mechanisms of these events that occur after assisted reproductive techniques.

Key words: dizygotic triplet pregnancy, monoamniotic twin, intracytoplasmic sperm injection, twin-to-twin transfusion syndrome

Introduction

Despite improvements in reproductive techniques, incidence of multiple gestation after assisted reproductive techniques (ART) is still very high. The known predisposing factors are; family history of multiple gestation, maternal age, parity, race, multiple embryos transferred and treatment with drugs that may stimulate multiple ovulation (1-5). Especially monozygotic triplets are very rare and they are reported to occur in 0.004% of all pregnancies (6). But the rates of perinatal risk in monochorionic twin pregnancies have been reported as 28-70% in literature (7). Particularly prematurity, congenital anomalies, rare vascular complications such as twin-twin transfusion syndrome, entangled, knotted or intertwined cords are shown as important reasons of increase in perinatal risk (7). The factors affecting the frequency of monozygotic twins (MZT) are not clear. In fact, all twins face certain risks. We present a case of dizygotic triplet pregnancy with monoamniotic twins subsequent to in utero transfer of three embryos.

Case

A 31-year-old nulligravida woman without any familiar twin tendency and having polycystic ovaries was admitted to our in vitro fertilization (IVF) unit for intracytoplasmic sperm injection (ICSI) cycle due to male factor infertility. Ovarian stimulation was performed with follicle stimulating hormone (Puregon, Schering-Plough, İstanbul, Turkey) and gonadotropin releasing hormone antagonist Ganirelix acetate (Orgalutran, Schering-Plough, İstanbul, Turkey). The daily dosage of gonadotropin was 225 IU/day and after 12 days of stimulation, 250 mcg Choriogonadotropin alfa (Ovitrelle®, Merck Serono S.A., Geneva, Switzerland) was applied.
with the plasma E2 level of 3085 pmol/L. The oocyte collection was performed 35 hours after the choriogonadotropin alfa application and 11 oocytes were transvaginally obtained. The number of M-II oocytes was nine and five of those were fertilized by using ICSI techniques. On the third day, three embryos (one grade I at the 8-cell stage, 2 of them grade II at the 6-cell stage) were transferred to the uterus. The luteal support was done with progesterone gel (CRINONE® 8% Progesterone Vaginal Gel, Serono Ltd, United Kingdom). Twelve days after the embryo transfer, the patient’s serum beta-hCG concentration was 448 mIU/mL. Transvaginal ultrasonographic (TVUS) demonstration of the viable embryo was done on the 6th week of pregnancy and showed three viable embryos in two gestational sacs in her uterus (Figure 1). The diagnosis was dizygotic triplet pregnancy. In the ninth week of pregnancy, dizygotic single fetus component died. So the pregnancy continued as a pregnancy of MZT. At 21 weeks of gestation, the patient was readmitted to our hospital for the management of threatened premature delivery and the ultrasound examination showed twin-to-twin transfusion syndrome (TTTS). At 22 weeks of gestation, the smaller fetus died. and three days later, premature rupture of the membranes occurred. TTTS was confirmed on histology. The birth weight of the recipient fetus was 625 g, while the birth weight of the donor fetus was 435 g.

**Discussion**

Twin gestations can be described as dizygotic and monozygotic (8-10). Dizygotic twins occur when two apart ova are fertilized by two apart sperms, but monozygotic twins occur by the division of the fertilized ovum after conception. Especially, monozygotic twinning is a rare pregnancy and the underlying mechanism is theoretically known. In monozygotic twinning, three time-points after fertilization are important. When the division of the embryonic cell mass occurs within 3 days of fertilization, diamniotic dichorionic gestations occurs. If division occurs between 4-8 days after fertilization, diamniotic monochorionic twins occur because chorion has already been developed by this time. If division occurs between 9-12 days following fertilization, monoaamniotic monochorionic gestations occur. In this situation, both the amnion and the chorion develop and the twins are surrounded by a common sac. Monoaamniotic monochorionic twinning is the rarest within monozygotic twin pregnancies. These situations are similar in twins after IVF/ICSI as well. (11). In 1984, the first cases of monozygotic twin pregnancy after IVF treatment were reported by Yovich et al (12). In our case, probably, one of the three transferred embryos was divided, the other was not implanted and a dizygotic triplet pregnancy occured. Namely, our case with dizygotic triplet pregnancy were composed of both dizygotic and monozygotic gestations. In addition to all this knowledge, simultaneous division of two or three transferred embryos is possible. In this condition multiple gestations such as quadruple gestation can occur. But, these are extremely rare and have more risk. The incidence of twins occurring naturally is 1 in 89 deliveries (9) and the monozygotic twinning shows in only 20% of these. While the incidence of MZT in all births is about 0.42%, the incidence of monozygotic triplets in all births is much lower as about 0.004% (6). In addition, monozygotic triplets account for only 4.5% of all triplet gestations (13). These rates are much higher in pregnancies occurring after ART. Yu Li at al. performed a Medline search of the literature from 1978-2009 and only found 11 case reports of monozygotic triplets after ART (14). In this circumstance, ART is estimated to increase the inci-
The real incidence of monozygotic twinning is difficult to estimate. Despite all this knowledge, the reason of the increased rates of monozygotic twinning after ART could not exactly be known and has been observed to be associated with many factors including the in vitro culture system, ovulation induction, zona hardening and assisted hatching, other zona manipulations such as ICSI that may affect the integrity of the zona pellucida, advanced female age and multiple embryo transfers performed to improve the success rate of pregnancy per cycle. Within these, zonal manipulation and multiple embryo transfer have been reported as the most important reasons. Sills et al. mentioned that micromanipulation is an independent risk factor for increased incidence of monozygotic twinning following ART. However, because very few case reports related with this problem were published until now, this complicated issue has still not been illuminated. So, larger numbers of samples are required to make a clear statement. In our case report, we didn't perform assisted hatching. The couple were young, had no family history of multiple pregnancies. However, three embryos were transfered on day 3 after ICSI and ovarian stimulation. Thus, the risk factors that could be associated with our case were ICSI and ovarian stimulation, and multiple embryo transfer.

In 1993, a dizygotic triplet pregnancy after IVF was first reported. Different from normal pregnant women, all twin pregnancies carry some additional risks. But, dizygotic triplet pregnancies have higher additional risks such as preterm labor and perinatal mortality. The most important reason for this is the presence of MZT. The increasing morbidity and mortality in monochorionic twins is due to the presence of placental vascular anastomoses, the increasing rate of congenital or chromosomal anomalies, premature birth, umbilical cord abnormalities such as umbilical cord entanglement and significantly growth discordant. The most important complication is TTTS. TTTS complicates 15%-30% of diamniotic monochorionic or monoamniotic twin pregnancies and accounts for 15%-17% of perinatal mortality. TTTS is the placental vascular anastomoses between the 2 fetuses. While there is hypovolemia, anemia, hypoxia, and growth retardation in the donor, there is polycythemia, polyhydramnios and hypervolemia with circulatory overload in the recipient. This is a vicious circle. Consequently, anemia and hypervolemia lead to brain damage or heart failure, and in conclusion to perinatal death. The death of one fetus, usually the donor, is associated with subsequent death of the other one. So, the early diagnosis and treatment of TTTS is important. On ultrasound, the early diagnosis of this situation can be achieved by colour doppler. The measurement of nuchal translucency in monochorionic multiple pregnancies may also be important for the early diagnosis of TTTS. But first, the diagnosis of monochorionic twin gestation has to be made with findings of the twin-peak or lambda sign. Recently, laser coagulation of arteriovenous anastomoses in the treatment of TTTS is performed and it is known as an effective treatment. The main goal during ART is to avoid all these complications. Therefore, efforts to diminish the rate of twin pregnancies that occur after ART are ongoing all over the world. Nowadays, reducing the number of embryos transferred in ART is the method preferred to reduce multiple pregnancy rates. In addition, fetal reduction is performed in multiple pregnancies with the component of MZT. In such twin pregnancies, neonatal outcome is better after selective embryo reduction. For a suitable choice, 11th week of pregnancy is usually preferred. But, timing of fetal reduction is also controversial. Because; 1) If this process is done during the second trimester, TTTS may harm the fetuses 2) If there is a fetus with chromosomal or structural anomalies, it can't be distinguished during the first trimester, 3) A small amount of KCl during fetal reduction raises the risk of co-twin loss due to the risk of transfusion of KCl to the co-twin. Our case was diagnosed at the 6th weeks of gestation as three viable embryos in two amniotic cavities, two of which were comprised in the same gestational sac. In the ninth week of pregnancy, the dizygotic fetus component died. So the pregnancy continued as a pregnancy of MZT. One of the monozygotic twins might have been planned to...
be sacrificed in the first trimester in order to minimize the risk of TTTS during pregnancy or laser ablation might have been performed for placental vascular anastomoses between the 2 fetuses. But, the patient did not receive follow-up. The patient was re-admitted at the twenty-second weeks gestation and the pregnancy was terminated due to TTTS.

In conclusion, the incidence of dizygotic or/and monochorionic triplet pregnancies following ART is approximately 10 times higher than normal. In dizygotic triplet pregnancies, both the mother and the fetus have higher risks of obstetric complications. Therefore, the couples must be informed before ART. In addition, the most significant contributing factor of the multiple pregnancy rate after ART is multiple embryo transfer. For that reason, it is important to lower the number of embryos at transfer. If possible, only one or two embryos should be transferred.

References


