Early prenatal diagnosis of multiple midline defects and limb anomalies in one fetus of triplets undergoing an in vitro fertilization program with laser-assisted hatching

Multiple midline defects (MMD) combined with limb anomalies are severe structural abnormalities with poor prognosis (Khoury et al., 1989). Prenatal diagnosis is mandatory for early detection and management. To date, prenatal diagnosis of MMD in one fetus of a triplet in early pregnancy has never been reported. In this communication, we have reported prenatal diagnosis of a case of MMD (encephalocele, omphalocele, cleft lip and palate) combined with scoliosis and clubfeet in one fetus of a triplet pregnancy revealed by a routine ultrasound scan at 16 weeks of gestation. The triplet pregnancy had been conceived by in vitro fertilization (IVF) with laser-assisted hatching (LAH). To the best of our knowledge, this may be the first such case.

A 37-year-old woman with primary unexplained infertility for seven years had undergone three cycles of IVF unsuccessfully. She underwent a new IVF program combined with LAH owing to the thickened zona of the embryo. On the third day after the IVF (i.e. at the eight-cell stage of the embryo), the reproductive specialists used a ‘noncontact’ infrared laser (1480 nm in wavelength) with 5 ms/shot for 3 shots to assist hatching. Immediately after LAH, three embryos were transferred into the uterine cavity smoothly.

A triplet pregnancy was then successfully implanted and developed. At 16 weeks of gestation, she was transferred to our department for prenatal ultrasound scanning. There were three fetuses with three chorions and three amnions in utero. Unexpectedly, we found one of the triplets to have MMD, including encephalocele (Figure 1a), omphalocele, cleft lip and cleft palate, scoliosis and clubfeet as well. Prenatal diagnosis of MMD with limb anomalies was made. In contrast, the other two fetuses were structurally normal.

Genetic counseling was given, and the couple decided to continue the triplet pregnancy. At 34 weeks of gestation, a Cesarean section was undertaken to deliver the three fetuses owing to preterm labor. The abnormal female fetus died soon after delivery. The other two fetuses (one male and one female) were grossly normal.

Figure 1—(a) Prenatal ultrasonography at 16 weeks of gestation revealed multiple midline defects (MMD) combined with limb anomalies. The figure shows the encephalocele. The large arrow indicates the brain tissue and the small white arrow indicates the orbital bone. (b) The gross findings of the anomalous female fetus with multiple midline defects (MMD) at autopsy. The figure reveals the cleft lip and cleft palate with encephalocele adhering to the placental tissue. (c) The figure shows the severe scoliosis, clubfeet and anterior abdominal wall defect.
and their birth weights and Apgar scores were 1810 g and 1818 g, 7 to 8 and 8 to 9 at 1 min and 5 min respectively.

Autopsy of the abnormal female baby confirmed our prenatal ultrasound findings of MMD, including encephalocele (Figure 1b), abdominal defect with omphalocele, cleft lip and palate, scoliosis and clubfeet (Figure 1c). The encephalocele adhered to the placenta, but the rest of the fetal parts were free. The final diagnosis after histopathological examination was MMD with limb anomalies. The karyotype of the dead anomalous female fetus was normal, 46, XX.

In general, MMD with limb anomalies is very serious and may be fatal. Some investigators reported an association of laterality and other complex midline anomalies, both resulting from a disturbance of pattern formation during blastogenesis (Gilbert-Barness et al., 2001). In our case, the LAH was performed to increase the implantation rate (Antinori et al., 1996). Whether LAH in an IVF program might disturb blastogenesis is unknown. Khoury et al. (1989) pointed out that the causes of midline defect associations may be due to Mendelian inheritance, chromosomal aberrations or drug exposure. Bird et al. (1994) reported that an autosomal gene might regulate the organization of midline structures. In our case, all the reviews of family history, obstetric history or any drug abuse were noncontributory. Therefore, the LAH procedure might be the only possible clue to induce the disturbance of blastogenesis and thus cause multiple midline defects. However, further studies on the association between LAH and MMD with limb anomaly are warranted.

In conclusion, prenatal diagnosis of MMD with limb anomalies in a triplet pregnancy at early pregnancy has never been reported. Furthermore, it has never been reported in a case of a triplet pregnancy undergoing an IVF program with LAH. Our case raises the possibility of causation of MMD with limb anomalies by LAH, which may deserve the attention of physicians, especially in the field of reproductive medicine.

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REFERENCES


