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Research Letter

Magnetic resonance imaging demonstration of sirenomelia in one fetus of a dizygotic twin pregnancy conceived by intracytoplasmic sperm injection, *in vitro* fertilization and embryo transfer

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A 32-year-old, primigravid woman presented with a twin pregnancy at 21 weeks of gestation for evaluation of oligohydramnios in one co-twin. The woman and her husband were healthy and non-consanguineous. There was no family history of congenital malformations, and the woman did not have diabetes mellitus. The woman had suffered from bilateral tubal occlusion and primary infertility. This was her first pregnancy that was conceived by intracytoplasmic sperm injection (ICSI), *in vitro* fertilization (IVF) and embryonic transfer (ET). Four embryos had been implanted and two survived. Level II ultrasound at 21 weeks of gestation revealed a normal co-twin and an abnormal co-twin with marked oligohydramnios, and absent kidneys and urinary tracts. Magnetic resonance imaging (MRI) evaluation of the fetuses at 31 weeks of gestation revealed a normal co-twin and an anomalous co-twin with oligohydramnios, pulmonary hypoplasia, a small stomach, ill-defined small bowel loops, absent bladder, renal agenesis and a single leg consistent with the diagnosis of sirenomelia (Fig. 1). The pregnancy was uneventful until 35 weeks of gestation when premature rupture of the membranes occurred. A 2128-g normal female co-twin and a 1576-g abnormal co-twin with a single lower extremity without the foot, an imperforate anus, absence of external genitalia and a single umbilical artery were delivered by cesarean section because of malpresentation. Postnatal X-ray examination of the abnormal infant showed sirenomelia with hypoplastic pelvis, absence of the right, lower limb and the left foot, and abnormal lumbosacral spine (Fig. 2). Cytogenetic analysis of the cord blood of the abnormal co-twin revealed a karyotype of 46,XX. A molecular zygosity test of the twins confirmed dizygotic twinning (Fig. 3). The abnormal co-twin died soon after birth (Fig. 4). The normal co-twin was doing well at the age of 4 months.

Sirenomelia is characterized by a complete or incomplete fusion of the lower extremities, imperforate anus and absent external genitalia, and can be associated with anomalies such as Potter syndrome, limb–body wall complex, pentology of Cantrell, esophageal atresia, hydrocephalus, holoprosencephaly, neural tube defects and VACTERL (vertebral segmentation defects, anal atresia/stenosis, cardiac malformation, tracheo-esophageal fistula and/or esophageal atresia, and renal and limb anomalies) association [1,2]. Sirenomelia has an overall incidence of 1.5–4.2/100,000 births and may be associated with maternal diabetes and monozygotic twinning [1,2]. About 2% of the cases with sirenomelia are associated with maternal diabetes, and there is a 100～150-fold increase in the incidence of sirenomelia in monozygotic twinning over that in singleton pregnancy and dizygotic twinning [1,2]. Recently, sirenomelia has been suggested as a primary defect

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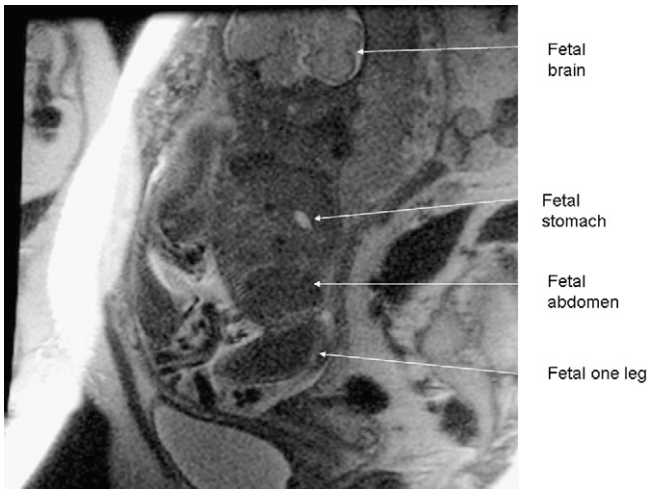

Fig. 1. Magnetic resonance imaging (MRI) at 31 weeks of gestation demonstrating a fetus with oligohydramnios, pulmonary hypoplasia, a small stomach, ill-defined bowel loops, absent bladder, agenesis of kidneys and a single leg consistent with the diagnosis of sirenomelia.

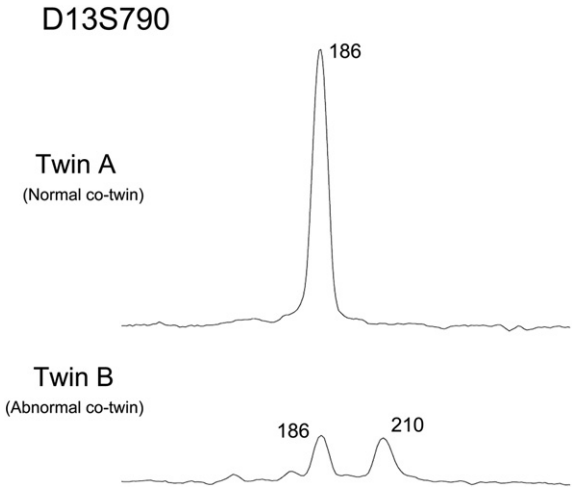

Fig. 3. Molecular zygosity test of the twins shows dizygostic twinning.

of blastogenesis affecting multiple primordial fields originating from the caudal mesenchyme [3−6].

We previously described limb−body wall complex in one fetus of a dizygotic twin pregnancy conceived by IVT-ET [7]. In this report, we additionally describe sirenomelia in one fetus of a dizygotic twin pregnancy conceived by ICSI and IVT-ET. Monozygotic twinning is well known to be associated with early embryonic structural developmental defects such as sirenomelia, holoprosencephaly, anencephaly, extrophy of the cloaca malformation and VATERR (vertebral defects, anal atresia, tracheo-esophageal fistula, esophageal atresia, and radial and renal dysplasia) association [8]. The majority of monozygotic twins with early embryonic structural developmental defects are discordant for anomalies, and only 5−20% of the cases are concordant [9]. About 15% of the cases with sirenomelia are reported to be associated with twin pregnancies, most often monozygotic twinning [10]. However, the present case was a dizygotic twin pregnancy. Dizygotic twin pregnancy has been shown to be associated with structural abnormalities in one fetus [11,12]. Sirenomelia has been reported in dizygotic twin pregnancy [13−16]. Sirenomelia has also been reported in the product of ICSI [17].

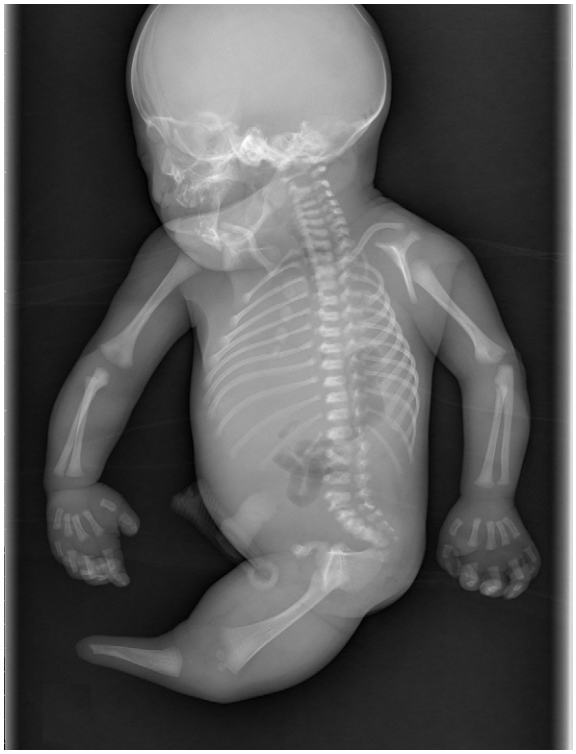

Fig. 2. Postnatal X-ray showing sirenomelia with hypoplastic pelvis, absent right lower limb, absent left foot and an abnormal lumbosacral spine with sacrococcygeal dysgenesis.

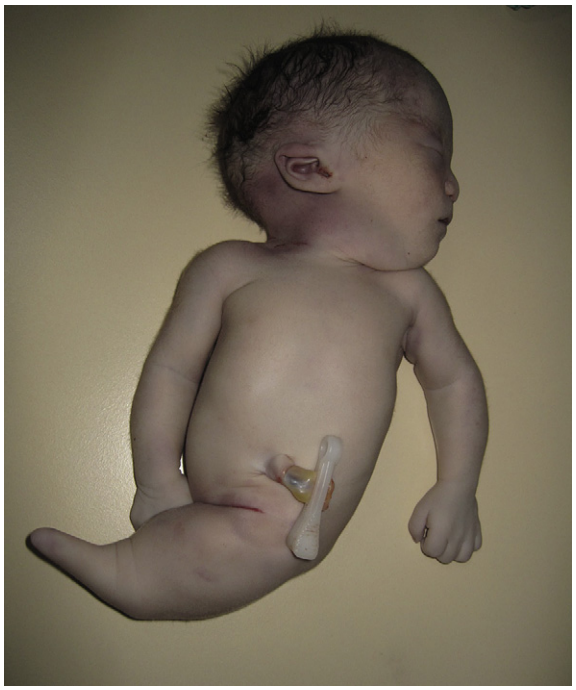

Fig. 4. The abnormal fetus with sirenomelia.

Sirenomelia in our case was likely to be related to developmental defects of the fetus. This case provides additional evidence for the occurrence of sirenomelia in multiple pregnancies after ICSI and IVF-ET with no influence of monozygosity and invasive prenatal diagnostic procedures of the pregnant woman.

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