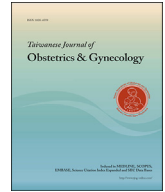




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Case Report

Prenatal diagnosis and management of monozygotic twins discordant for severe fetal abnormalities

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ABSTRACT

Objective: We present prenatal diagnosis and management of monozygotic (MZ) twins discordant for severe fetal abnormalities.**Case report:** A 36-year-old woman underwent amniocentesis at 18 weeks of gestation because of advanced maternal age, and hydrops fetalis, a giant cystic hygroma of 5 × 3.5 cm and left hydronephrosis in a co-twin. The other co-twin was structurally normal. Amniocentesis revealed a karyotype of 46,XY in both co-twins. Simultaneous polymorphic DNA marker analysis using the DNAs extracted from maternal blood and uncultured amniocytes confirmed MZ twinning. The woman underwent a successful selective fetal reduction by radiofrequency ablation at 22 weeks of gestation. At 28 weeks of gestation, premature rupture of membranes occurred, and a 1280-g normal male baby and a 275-g dead malformed co-twin were delivered. The normal co-twin was phenotypically normal and was doing well at age seven weeks. **Conclusions:** Prenatal diagnosis of MZ twins discordant for structural abnormalities should include a differential diagnosis of MZ twinning, and a zygosity test is necessary under such a circumstance.© 2020 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

We previously reported prenatal diagnosis of monozygotic (MZ) twinning discordant for chromosomal aberration at amniocentesis [1]. Here, we present a pregnancy with MZ twinning discordant for severe fetal abnormalities.

Case report

A 36-year-old, gravida 5, para 2, woman underwent amniocentesis at 18 weeks of gestation because of advanced maternal age, and hydrops fetalis, a giant cystic hygroma of 5 × 3.5 cm and

left hydronephrosis in a co-twin. The other co-twin was structurally normal. Her husband was 37 years old. The couple has two healthy daughters, and there was no family history of congenital malformations. She did not undergo any assisted reproductive technology during this pregnancy. Amniocentesis revealed a karyotype of 46,XY in both co-twins. Simultaneous polymorphic DNA marker analysis by quantitative fluorescent polymerase chain reaction (QF-PCR) using the DNAs extracted from maternal blood and uncultured amniocytes confirmed MZ twinning (Table 1). The woman underwent a successful selective fetal reduction by radiofrequency ablation (RFA) at 22 weeks of gestation (Fig. 1). At 28 weeks of gestation, premature rupture of membranes occurred, and a 1280-g normal male baby and a 275-g dead malformed co-twin were delivered. The normal co-twin was phenotypically normal and was doing well at age seven weeks. His body weight was 1960 g.

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Table 1

Genotypic information of the twins and mother at small tandem repeat markers specific for chromosomes 13, 18 and 21 obtained by quantitative fluorescent polymerase chain reaction assays^a.

Markers	Locus	Mother	Twin A	Twin B
D13S893	13q12.3	186, 186	186, 186	186, 186
D13S789	13q22.3	163, 167	163, 163	163, 163
D18S869	18q11.2	186, 190	186, 190	186, 190
D18S535	18q12.3	128, 128	128, 128	128, 128
D21S1432	21q21.1	128, 144	128, 140	128, 140
D21S1437	21q21.1	115, 135	135, 135	135, 135

^a Alleles (basepair sizes) are listed below each individual.

Discussion

Structural abnormalities occur more often in MZ twins compared with singletons with a relative risk of 1.25 (95% confidence interval, 1.21–1.28) for congenital anomalies in MZ twins compared with singletons [2]. Structural abnormalities also occur more often in MZ twins compared with dizygotic (DZ) twins with a relative risk of 1.4–2.7 for congenital anomalies in MZ twins compared with DZ twins [3–5]. In a study of 945 twins, Sperling et al. [6] found that the incidence of structural malformation was 3.2% among MZ twins and 2.2% among DZ twins.

The present case was associated with MZ twins discordant for cystic hygroma, hydrops fetalis and unilateral hydronephrosis. MZ twins have been reported to be associated with various structural abnormalities such as cystic hygroma [7], anencephaly and Cantrell syndrome [8], lateral open cranial defect [9], pure XY gonadal dysgenesis and agenesis [10], vaginal agenesis and bilateral tibial longitudinal deficiency [11], VACTERL association [12], primary ciliary dyskinesia and organ laterality [13], left microtia [14], congenital heart defects [15–17], congenital diaphragmatic hernia and esophageal atresia [18], hemifacial microsomia [19], cloacal anomaly [20,21], body stalk anomaly [22] and semilobar

holoprosencephaly [23]. In a review of 77 monochorionic diamniotic twins discordant for structural abnormalities, Wang et al. [24] found that 32% were neurological malformations, 29% were cardiovascular malformations and 10% were twin reversed arterial perfusion sequence.

Prenatal diagnosis of MZ twins discordant for lethal structural abnormalities should raise a concern of the effect of single fetal death in MZ twins on pregnancy outcome and fetal brain injury in survivors of twin pregnancies complicated by demise of one twin [25]. Hillman et al. [26] found that following single intrauterine fetal death, the surviving monochorionic twins were more likely to have postnatal abnormal cranial ultrasound and neurodevelopmental morbidity than dichorionic twins with a comparison of occurrence rate of 34% vs. 16% in abnormal cranial ultrasound and a comparison of occurrence rate of 26% vs. 2% in neurodevelopmental morbidity, respectively. O'Donoghue et al. [27] found that the gestation age of single fetal death in twin pregnancies before 28 weeks and after 28 weeks is a prognostic factor of brain injury with a comparison of occurrence rate of 3.6% vs. 20%. There is because of larger placental anastomoses and greater impact of exsanguination after 28 weeks. In order to prevent the risk of brain injury of the normal co-twin in case of discordant lethal congenital abnormalities, selective reduction of the abnormal co-twin by a selective cord occlusion technique such as RFA has the advantage of preventing from massive exsanguination in case that the abnormal co-twin dies suddenly which leads to brain injury in the normal co-twin. In the presence of twin-to-twin circulation, if intrauterine fetal death occurs in one co-twin, there is acute transplacental exsanguination of the living fetus into the circulation of the demised co-twin [28].

The peculiar aspect of the present case is simultaneous determination of zygosity during amniocentesis for cytogenetic analysis for chromosomal abnormality of the fetus, and the correct choice of the selective cord occlusion technique for selective reduction of the abnormal fetus. In the pregnancy with MZ twins discordant for

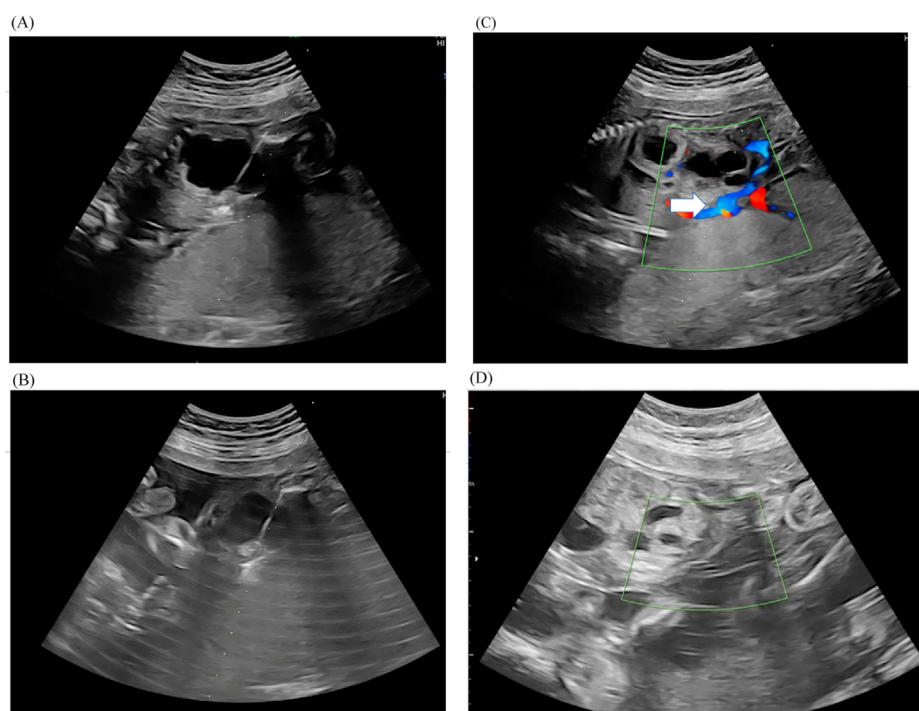


Fig. 1. The application of selective fetal reduction by radiofrequency ablation (RFA) of the umbilical cord of the malformed fetus at 22 weeks of gestation. (A) Puncture of the needle, (B) RFA, (C) blood flow before RFA and (D) no flow after RFA.

structural abnormalities, selective fetal reduction by intracardiac injection of potassium chloride should not be performed in the presence of twin–twin circulation. Currently, various selective cord occlusion techniques such as RFA, laser cord occlusion and bipolar cord coagulation are applicable under such a circumstance. RFA has been shown to be a reliable option for selective fetal reduction in monochorionic multiple pregnancies [29,30]. In a retrospective study of 156 patients of complex multiple pregnancies treated with RFA for selective fetal reduction, Meng et al. [29] found a 17.3% (27/156) rate of miscarriage, a 7.1% (11/156) rate of intrauterine fetal death, a 75.6% (118/156) rate of overall survival and a 19.5% (23/118) rate of premature birth before 34 weeks of gestation. In a retrospective study of 84 cases (174 fetuses) of complex monochorionic pregnancies treated with RFA for selective fetal reduction, Shi et al. [30] found a 21% (18/84) rate of miscarriage and intrauterine fetal death, a 10% (8/84) rate of termination of pregnancy because of fetal malformation or oligohydramnios and a 69% (58/84) rate of total live birth with a mean gestation age at delivery of 35 weeks. In the present case, we used QF-PCR assays for rapid determination of zygosity which has been proven to be a useful tool for rapid determination of zygosity [31]. Prenatal diagnosis of twins discordant for structural abnormalities should alert the possibility of MZ twinning, and QF-PCR testing is useful for rapid determination of zygosity under such a circumstance.

In summary, we present prenatal diagnosis and management of MZ twins discordant for severe fetal abnormalities. Prenatal diagnosis of MZ twins discordant for structural abnormalities should include a differential diagnosis of MZ twinning, and a zygosity test is necessary under such a circumstance.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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