Table 4 Logistic regression for donor fetal demise

	IUFD ($n = 18$)	Live-birth ($n = 34$)	Univariate analysis Odds ratio (95% CI)	*P*-values	Multivariate analysis Odds ratio (95% CI)	*P*-values
DVARF	5 (28%)	1 (3%)	12.7 (1.35–119)	0.015		0.050
PUVF	3 (17%)	1 (3%)		0.110		0.18
AA	14 (78%)	4 (9%)	5.00 (1.36–18.4)	0.019		0.08
VV	5 (28%)	5 (15%)		0.287		0.31
Modified SQLPCV	3 (17%)	20 (59%)	0.14 (0.034–0.58)	0.007	0.09 (0.016–0.57)	0.01
Discordant rate >25%	13 (82%)	21 (75%)		0.72		–
EFW < –2SD	8 (50%)	16 (57%)		0.757		–

Abbreviations as in Tables 1 and 2. Data are presented as number (%) or median (range).

IUFD occurred in two modified SQLPCV group cases (18%); this finding was significantly lower than that of the SLPCV group (70.6%; $P = 0.018$). If AA anastomoses were present, ratio of donor IUFD was significantly higher than that in the cases without AA anastomoses in the SLPCV group ($P = 0.025$), but not in the modified SQLPCV group. In regard to the recipients, the modified SQLPCV did not significantly improve fetal survival; however, there was only one IUFD in the group. Consequently, the overall IUFD rate per fetus was significantly lower in the modified SQLPCV group than that of the SLPCV group (9% vs 38%; $P < 0.001$); this finding was independent of the presence or absence of AA anastomoses. Multiple logistic regression analysis showed that the modified SQLPCV significantly reduced donor IUFD; however, no other factors contributed to IUFD in donors with UA-AREDF (Table 4). In regard to the recipients, any covariate was not associated with recipient IUFD (data not shown).

Discussion

This study shows that modified SQLPCV is useful for the prevention of fetal demise in cases of TTTS in which the donor had UA-AREDF. The number of overall IUFD per fetus was significantly decreased in patients who underwent SQLPCV rather than SLPCV (9% vs 38%; $P < 0.001$). This decreased rate of overall IUFD was primarily due to the decreased rate of donor IUFD.

Recently, Quintero *et al.*[10] presented the potential efficacy of sequential coagulations in AV anastomoses (SQLPCV). The difference between SLPCV and SQLPCV involves basing the decision to coagulate placental anastomoses in a phased manner on the types of anastomoses present. The SQLPCV was developed for the purpose of adjusting imbalanced blood flow volume between two fetal circulations even during the laser procedure itself, essentially designed to preserve blood flow volume in donors by coagulating all AVDR prior to AVRD. The umbilical blood flow (UBF) of donors in TTTS was significantly lower before laser surgery than it was following surgery.[23,24] Recently, Becker *et al.*[25] reported that, when compared with uncomplicated monochorionic twins, a significant decrease in donor UBF in donors was seen only at stage III or IV. They also reported a significant increase in UBF in recipients regardless of the stage of severity. These findings indicate that, in our study, the donor was hypovolemic or the recipient was hypervolemic before the laser surgery because a markedly abnormal Doppler (UA-AREDF) was seen in all cases. Although it was impossible to measure the direction and volume of blood transfused through AV anastomoses in the course of laser surgery, the significant improvement of overall fetal survival in modified SQLPCV may reflect not only the potential increase in donor blood flow but also the potential decrease in recipient blood flow. In particular, a significant improvement of fetal survival in cases without AA anastomoses may reflect the potential benefit of the sequential coagulation of all AVDR prior to AVDR because the influence of blood flow through AA anastomoses can be disregarded and the result supports the Quintero's original concept.

In cases with AA anastomoses, modified SQLPCV, obliteration of AA anastomoses prior to any other type of anastomosis, is more likely to prevent IUFD of donors with UA-AREDF compared with the SLPCV group. The presence of AA anastomoses has been considered to play a protective role against the development of TTTS in monochorionic pregnancies.[26] It has also been reported that detection of AA anastomoses by ultrasonography in fetuses who developed TTTS could confer a survival advantage[27] and that the detection at treatment could increase the chance of perinatal

survival, independent of stage.[28] However, the management consisted of conservative treatments such as amnioreduction and septostomy in the former report; laser surgery was performed in only three of 95 cases in the latter report. As the prognosis for AA anastomoses treated with laser surgery is currently unclear, it is necessary to clarify the role of AA anastomoses on the prognosis of fetuses following laser surgery. Murakoshi *et al.*[29] indicated that AA anastomoses could behave as functional AV anastomoses, in which a hemodynamic equator, a collision front between opposing blood flows along the AA anastomoses, displaced toward one side or the other depending on the pressure gradient between two fetuses. We speculated that an acute net transfusion via the direct communication of arteries could occur, depending on the pressure gradient between the fetuses, and considered that even a small change in the pressure gradient between the two fetuses following coagulation of AV anastomoses might cause a significant blood flow exchange via AA anastomoses while the anastomoses were still patent, which could result in a deterioration of hemodynamic status in both the hypotensive donor and the hypertensive recipient. The risk of patent AA anastomoses after coagulation of AV anastomoses may be explained in part by the following hypothesis. Removal of hypotension in the donor twin following coagulation of AV anastomoses may displace the hemodynamic equator toward the recipient's side, and the blood flow from the donor twin could enter the drainage vein into the recipient twin if the hemodynamic equator would displace beyond the confluence of the drainage vein; thus, transforming the AA anastomoses into a functional AVDR. Consequently, the donor may rapidly lose a significant amount of blood through the functional AVDR, which could aggravate the hypotensive or hypovolemic status of the donor. Conversely, when the hemodynamic equator displaces toward the donor's side secondary to the donor's progressive hypotension, the condition may worsen unless AA anastomoses work as a functional AVRD. Considering the fact that 86% of fetuses survived *in utero* after initial obliteration of AA anastomoses by modified SQLPCV, our hypothesis seems to be feasible.

This study had several limitations. First, the study population was limited to cases with UA-AEDF in the donors. As the primary purpose of the study was to elucidate the efficacy of modified SQLPCV on postoperative fetal survival, the high mortality rate, which has been noted in the subset of donors with UA-AREDF,[11–14] could become a useful indicator of the procedure's efficacy. It is unclear whether this modified method is effective in cases without donor UA-AREDF; therefore, further investigation is indicated. Second, another potential limitation is the sequence of coagulation in the SLPCV group, in which we included any cases incompatible to the sequence or included cases without a precise description of the sequence. However, considering the overall survival rate above 80% for at least one fetus in SLPCV, we assume these limitations are unlikely to affect the main conclusion. Third, we admit that this technique is a modification of a currently proposed technique by Quintero *et al.*, and the sequence of coagulation in the modified SQLPCV is correspondent to SQLPCV if the superficial anastomoses are absent. In this study, we dared to use the term 'modified SQLPCV' in all categorized cases because the procedure was intended prior to the treatment. Fourth, it is still unclear whether modified SQLPCV might be superior to SQLPCV. As this study was limited to the case with UA-AREDF, this result could not be comparable to the previous study of SQLPCV reported by Quintero *et al.* Thus, we can only say that modified SQLPCV is more efficacious than SLPCV not but SQLPCV. Further studies are needed in order to determine the optimal sequence.

In conclusion, modified SQLPCV, which may both preserve blood flow volume in donor twins and prevent an acute net transfusion via AA anastomoses, can improve fetal survival rate in TTTS with UA-AREDF in the donor. This study is a preliminary report and the rationale behind the procedure is a matter for speculation; however, we believe that utilization of the procedure could improve the outcome for fetuses with TTTS.

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Two cases of reversal of twin-twin transfusion syndrome diagnosed by measuring hourly fetal urine production

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Abstract

Reversal of twin-twin transfusion syndrome (TTTS) is a rare complication of monochorionic pregnancy. Diagnostic criteria and satisfactory therapeutic options have not been reported. We make a suggestion of diagnosis and therapy for reversal of TTTS. We report two cases of reversal of TTTS. Measurement of the fetal urine production rate was useful for management and better comprehension of the cases. In case 1, double intrauterine fetal demise occurred before the criteria for TTTS were fulfilled, in which each fetal urine production rate reversed prior to the change of amniotic fluid volume. In case 2, elevated urine production was noted prior to progressive polyhydroamnios and congestive heart failure in the new recipient and the fetoscopic laser photocoagulation of the placental communicating vessels was performed successfully before the criteria for TTTS were fulfilled. Both infants required intensive care, but developed normally and showed no neurologic complications at 2 years after birth. Hourly fetal urine production rate was useful for immediate diagnosis of reversal of TTTS, and laser photocoagulation of the placental communicating vessels is thus a method for the correction of the fetal blood flow imbalance in cases of reversal of the donor-recipient phenotype in TTTS.

Key words: hourly fetal urine production, monochorionic twin, reversal of twin-twin transfusion syndrome, twin-twin transfusion syndrome.

Introduction

Twin-twin transfusion syndrome (TTTS) is defined sonographically as the presence of polyhydramnios in the sac of one twin and oligohydramnios in the sac of the other twin. This typical feature of TTTS is thought to be caused by an imbalance in net blood flow through the placental communicating vessels on the surface of the monochorionic placenta. Several cases of reversal of the donor-recipient phenotype have been reported.[1,2] The pathophysiology, incidence, and optimal treatment options for reversal of TTTS are unclear. However, it is reported that once reversal of TTTS occurs, especially before 26 weeks of gestation, the perinatal prognosis is poor.[1–3] We report two cases of reversal of TTTS; one case had a poor outcome of double intrauterine fetal demise, but the other had a favorable outcome of double fetal survival as a result of early intervention by fetoscopic laser photocoagulation of the placental communicating vessels.

Case Reports

Case 1

A 27-year-old primigravida woman was referred to our hospital at 22 weeks and 1 day of gestation for evaluation of a complicated monochorionic diamniotic twin pregnancy with amniotic fluid discordance. Initial ultrasound examination showed 17.5% discordance in

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estimated fetal weight (EFW), in which the EFW of twin A was 496 g, and the EFW of twin B was 409 g, without structural abnormalities. The maximum vertical pocket (MVP) of the amniotic cavity differed distinctly between the fetuses (the MVP of twin A was 9.2 cm; the MVP of twin B was 2.2 cm). TTTS was suspected, in which twin A was considered the recipient fetus and twin B the donor fetus. But the MVP of twin B was more than 2 cm, the criteria of TTTS was not fulfilled and fetoscopic laser photocoaglation was not indicated. Doppler ultrasonography showed no critically abnormal Doppler waveforms, such as absent end-diastolic flow in the umbilical artery (UA-AEDF), reversed flow during atrial contraction in the ductus venosus (DV-RF) or pulsatile umbilical venous flow (PUVF) in either fetus. Despite polyhydramnios, the bladder of twin A was small, whereas the bladder of twin B was large, despite oligohydramnios. The hourly fetal urine production rate (HFUPR) was estimated by ultrasonography as described by Rabinowitz *et al.*[4] Measurements were made with ultrasonic calipers at 5 min intervals for 1 h. The greatest longitudinal bladder view was identified and measured to estimate bladder volume. The slope of the filling phase, calculated by regression analysis, is used to estimate the hourly fetal urine production rate. Contrary to the presence of polyhydramnios in twin A and oligohydramnios in twin B, the HFUPR for twin A was 1.4 mL/h, and that for twin B was 11 mL/h, suggesting oliguria in twin A and polyuria in twin B. Daily ultrasound examinations documented a gradual decrease of amniotic fluid in twin A and a sudden increase of amniotic fluid in twin B (Fig. 1), which was interpreted as reversal of TTTS. At 22 weeks and 6 days of gestation, typical features of congestive heart failure were observed in twin B, who showed DV-RF and cardiomegaly in addition to progressive polyhydramnios. The MVP of twin A decreased to the lowest limit of the normal range due to persistent oliguria. Although reversal of TTTS was strongly suspected, the MVP in twin A was maintained at greater than 2 cm, which did not fulfill the criteria for fetoscopic laser photocoagulation for TTTS at our institution at that time. At 23 weeks and 2 days of gestation, the status of twin B deteriorated, and included UA-AEDF with DV-RF and ascites. Fetal demise of twin B occurred on the same day. To prevent potential perimortem feto-fetal transfusion, intrauterine rescue transfusion was attempted, but twin A also died. Twin A was 488 g and pale, and twin B was 676 g and plethoric at birth. Pathologic examination of the placenta showed a single artery-to-artery (AA) anastomosis and two artery-to-venous (AV) anastomoses from twin B to twin A on the surface of the chorionic plate.

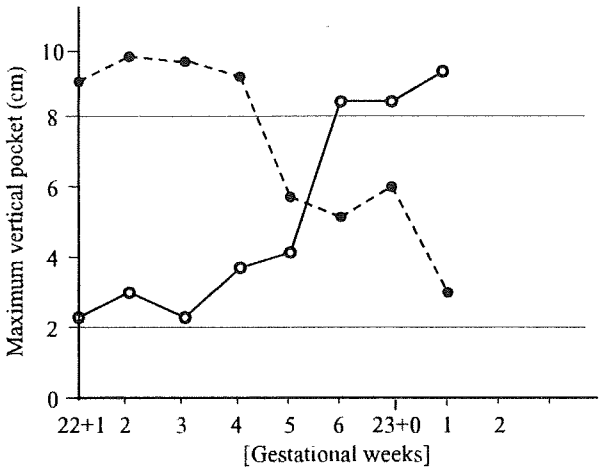

Figure 1 Changes in the maximum vertical pocket (MVP) of twin A (●) and twin B (○) in case 1. Daily ultrasound examinations documented a gradual decrease of amniotic fluid in twin A and a sudden increase of amniotic fluid in twin B.

Case 2

A 25-year-old primigravida woman was referred to our hospital at 19 weeks and 5 days of gestation for evaluation of amniotic fluid discordance in a monochorionic diamniotic twin pregnancy. Initial ultrasound examination showed polyhydramnios in one twin and most likely oligohydramnios in other twin (MVP of twin A was 8.6 cm, and MVP of twin B was 2.5 cm). No structural abnormalities or abnormal Doppler waveforms were observed at that time. Serial ultrasound examinations, including Doppler study and estimation of HFUPR were conducted. Polyhydramnios in twin A gradually improved as the urine production rate decreased, whereas polyhydramnios in twin B progressed as the urine production rate increased dramatically (Figs 2,3). At 22 weeks of gestation, typical features of congestive heart failure, including DV-RF, PUVF, and cardiomegaly, were observed in twin B, who was considered the initial donor and present recipient. Upon diagnosis of reversal of FFTS, laser surgery was considered and approved by the Institutional Review Board in our hospital. After extensive counseling regarding the diagnosis, possible outcomes, and alternative therapeutic options, including expectant management, amnioreduction, and laser

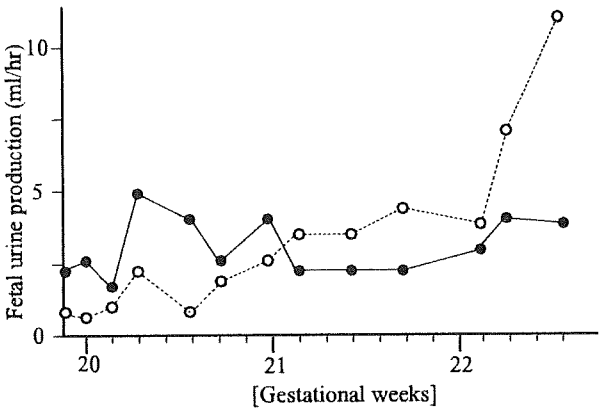

Figure 2 The solid line shows changes in fetal urine production of twin A (●) and the dashed line shows that of twin B (○) in case 2. The urine production rate in twin A gradually decreased, whereas that in twin B dramatically increased.

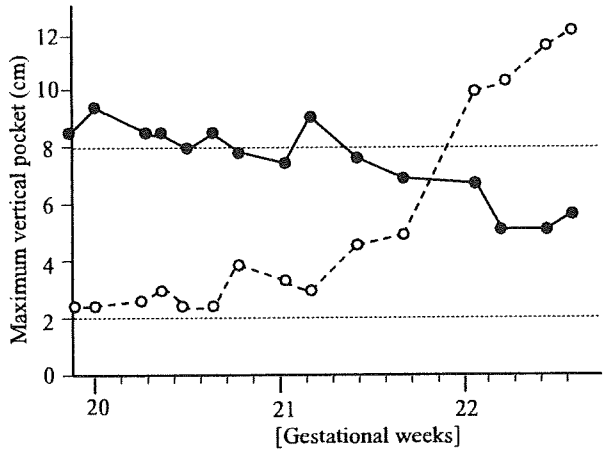

Figure 3 The solid line shows changes in the maximum vertical pocket (MVP) of twin A (●) and the dashed line shows MVP of twin B (○) in case 2. Polyhydramnios in twin A was gradually improved as the urine production rate decreased, whereas polyhydramnios in twin B progressed as the urine production rate increased dramatically.

surgery, the patient and her family provided written informed consent for laser surgery. At 22 weeks and 4 days of gestation, fetoscopic laser photocoagulation of the placental communicating vessels was performed as described previously.[5] In brief, a small skin incision was made under both local and intravenous anesthesia. Under ultrasound guidance, a 3.8-mm trocar (Richard Wolf Medical Instruments, Vernon Hills, IL, USA) was introduced into the sac of twin B. Fetoscopic observation with a 3.3-mm diagnostic endoscope (Richard Wolf Medical Instruments) showed only two anastomoses in the placental surface between the two fetuses, one AV anastomosis from twin A to twin B and another AV anastomosis in the opposite direction. The two vascular anastomoses were of a similar size. A 550-μm neodymium: YAG laser fiber (SlimLine; Lumenis Japan, Tokyo, Japan) was inserted through the operating channel of a 3.3-mm operating endoscope (Richard Wolf Medical Instruments), and all anastomoses were photocoagulated. Two days after surgery, signs of congestive heart failure (DV-RF and PUVF) in twin B diminished, and polyhydramnios had not progressed. The patient delivered two female infants (twin A weighed 999 g and twin B weighed 995 g), by emergency cesarean section because of placental abruption at 27 weeks and 4 days of gestation. The pathological examination of the delivered placenta was consistent with fetoscopic findings and both anastomoses had no patency. Both infants required mechanical ventilation in the neonatal intensive care unit for 1 week due to respiratory disorders, but no neurologic complications, such as intracranial hemorrhage or periventricular leukomalacia, were detected by serial cranial ultrasound studies. The neonatal courses of these infants were uneventful. Both children developed normally and showed no neurologic complications at 2 years after birth.

Discussion

Recently, Wee *et al.*[3] reported five cases of reversal of TTTS diagnosed by reversal of the donor-recipient phenotype; that is, a donor acquiring the features of a recipient and vice versa, and with 30% of perinatal mortality, while double fetal demises occurred in other reports.[1,2] Results of case 2 show the usefulness of fetoscopic laser photocoagulation of the placental communicating vessels for the treatment of reversal of TTTS. Although the pathophysiology of reversal of TTTS is unclear, anastomoses on the monochorionic placenta between the two fetal circulations are the cause of the acute hemodynamic changes seen in the new recipient and new donor. We began to use laser surgery to ameliorate the reversed blood flow imbalance between fetuses, even in cases in which the amniotic fluid in the new donor did not decrease enough to fulfill the diagnostic criteria for typical TTTS. Laser surgery has recently been indicated not only for TTTS, but also for other complications of monochorionic twin pregnancies, such as selective growth restriction[6] and twin

reversed arterial perfusion sequence,[7] in which the placental communicating vessels are involved. Reversal of TTTS may not meet the diagnostic criteria for typical TTTS, but ablation of the communicating vessels is reasonable, considering the potential adverse outcome of this complication.

Only a few reports have been published,[1,2,8] but the incidence and cause of reversal of TTTS are still unknown. Wee *et al.* reported reversal of the donor-recipient phenotype in five of 96 cases of TTTS.[3] At a similar incidence, we encountered the present two cases in the last 3-year period, during which 62 cases of TTTS had been evaluated at our hospital (unpubl. data). Serial ultrasound follow-up is necessary to detect the reversal of TTTS. It is still unclear which placental angio-architecture can cause reversal of TTTS, but paucity of placental anastomoses could attribute to the pathophysiology.[3] Only three communicating vessels in case 1 and two in case 2 were shown. We also conclude that hypotension of the donor and the existence of a large AA anastomosis may explain the reversal of phenotype. However, AA anastomosis seems not to be requisite to the hemodynamic alteration because of no AA anastomosis in case 2.

Measurement of fetal urine production rate was useful in the precise evaluation of urine production in both the hypervolemic and hypovolemic fetuses. Preceding the fluctuations in amniotic fluid volume, the urine production rate had already changed in both fetuses. The new recipient twin developed progressive polyhydramnios as the urine production rate increased. However, the MVP of the new donor sac did not fulfill the diagnostic criteria for oligohydramnios because of the preexisting polyhydramnios. The assessment of the urine production rate may reflect fetal hypervolemia and hypovolemia more precisely than assessment of amniotic fluid volume.

In conclusion, laser photocoagulation of the placental communicating vessels can be used to correct the blood flow imbalance between fetuses with reversal of the donor-recipient phenotype in TTTS.

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Prenatal spontaneous disruption of the dividing membrane in monochorionic diamniotic twins detected at the time of fetoscopic laser photocoagulation

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Abstract

Spontaneous antepartum rupture of the dividing membrane occurring in monochorionic diamniotic twins (MD twin) is an extremely rare complication and difficult to diagnose prenatally. We present a case of pseudo-monoamniotic twins derived from an MD twin gestation, which was suspected by ultrasound and was confirmed by antepartum fetoscopy. A 28-year-old woman, gravida 1, para 1 at 24 weeks of gestation was referred because of suspected polyhydroamnios in an MD twin. Ultrasound suggested twin–twin transfusion syndrome stage III, spontaneous rupture of the dividing membranes and cord entanglement. Fetoscopic laser photocoagulation (FLP) was performed using the Nd:YAG laser on 12 placental vascular connections. Fetoscopy revealed the spontaneous rupture of the dividing membrane and cord entanglement. The remainder of the pregnancy was managed as a monoamniotic twin gestation. Elective cesarean section was performed at 32 weeks of gestation following antenatal steroids and concordantly grown healthy male infants were delivered.

Key words: fetoscopic laser photocoagulation, monoamniotic twin, twin–twin transfusion syndrome.

Introduction

Monoamniotic twin gestations, which represent approximately 1% of all twins,[1] have a high perinatal mortality rate (30–70%), with the most common cause of fetal death being cord entanglement.[2] Chorionicity is usually determined by ultrasonography in the first trimester of pregnancy. In rare cases, MD twin gestation diagnosed in the first trimester converts spontaneously to monoamniotic twins as a result of *in utero* disruption of the dividing membrane. Pseudo-monoamniotic twins have been reported previously and their perinatal mortality rate would be equivalent to that of original monoamniotic twins. Although pseudo-monoamniotic twins were reported previously, they were all suspected prenatally by ultrasound and were detected by the macroscopic and pathological findings after birth.[3–12] Meanwhile, fetoscopic laser photocoagulation for placental communicating vessels (FLP) has recently emerged as a treatment option for twin–twin transfusion syndrome (TTTS), which is usually performed before 26 weeks of gestation. We report the first case of constructive monoamniotic twins resulting from an original MD twin gestation antenatally, of which disruption of the dividing membrane was detected prenatally at the time of FLP for the treatment of TTTS.

Case Report

A 28-year-old woman, gravida 1, para 1, was initially diagnosed with monochorionic diamniotic twin (MD twin) pregnancy by ultrasonography in the

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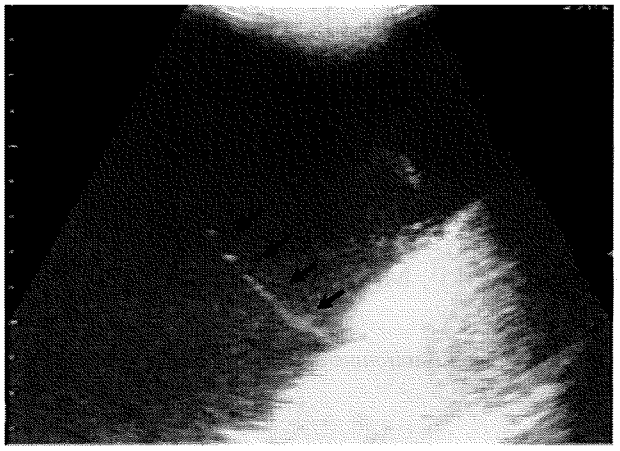

Figure 1 Transabdominal ultrasonography at 24 weeks of gestation shows the 'thin' dividing membrane from the chorionic surface of the posterior placenta (arrows).

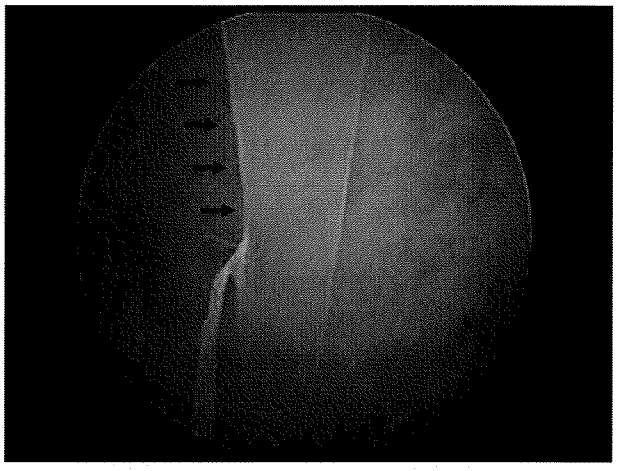

Figure 2 Fetoscopic finding at 24 weeks of gestation of a short falciform remnant of dividing membranes with an irregular margin (arrows).

first trimester of gestation. A dividing membrane and equal amniotic fluid volume in each sac were noted. At 24 weeks of gestation, the twins were found to have polyhydramnios and threatened premature labor with abdominal distention and pain, therefore the patient was transferred to our hospital. Ultrasonography showed a relatively thin dividing membrane with a free-floating edge, mainly close to the chorionic surface of the posterior placenta (Fig. 1). Although the twins obviously had polyhydramnios with 8.4 cm of maximum amniotic fluid pocket, each amniotic fluid pocket was difficult to measure due to the unclear membrane. Estimated fetal weights were 560 g and 720 g. The bladder could not be identified in the smaller fetus and was distended in the larger fetus. A diagnosis of TTTS stage III was made because of an absent end-diastolic flow in the umbilical artery of the larger fetus. On the same day, the patient was referred to the perinatal care center of Yamaguchi University for FLP. Fetoscopy disclosed spontaneous rupture of the dividing membrane (Fig. 2) and cord entanglement. The insertion sites of the two umbilical cords were contiguous, and a short falciform remnant of the disrupted intervening membrane was seen on the placenta between the umbilical cords. Twelve placental vascular communications were coagulated by Nd:YAG laser, and about 3300 mL of amniotic fluid were aspirated. Both fetuses developed transient hydrops, which disappeared at 11 days after FLP. The fetal weight discordancy of the twins resolved gradually. At 26 weeks of gestation the patient was admitted to our hospital for surveillance. Elective cesarean

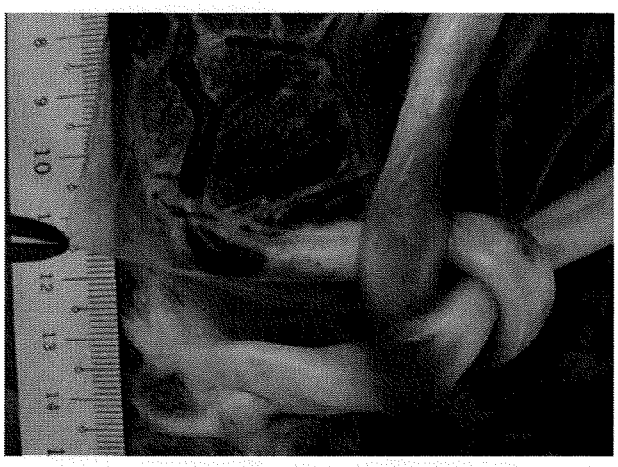

Figure 3 Photograph of the placenta showing contiguous cord insertion sites and a thin short dividing membrane with loose cord entanglement.

section was performed at 32 weeks of gestation following administration of maternal antenatal steroids, and concordant male infants with loosely entangled umbilical cords weighing 1762 g and 1744 g were delivered from a single gestational sac, with an Apgar score of 8 and 9 at 1 and 5 min in each twin. Gross pathological examination showed that the placenta had a dividing membrane between the cord insertions (Fig. 3). The patient's postoperative course was uneventful and the mother and her infants were discharged on postoperative days 8 and 36, respectively.

Discussion

We were able to find 10 articles reporting 17 cases of pseudo-monoamniotic twins derived from MD twins and their perinatal mortality rate is thought to be equivalent to original monoamniotic twins.[3–12] Trauma or physical rupture by the fetuses have been entertained as possible etiological factors.[3] Other possible causes include amniocentesis,[3,6,7] cordcentesis,[5] and other invasive intrauterine procedures.[3] Infection, developmental disturbances,[3] and intrauterine sling formation are other possible causes. Among these proposed causes, intrauterine invasive procedures are the most frequently reported.

We report the first case of pseudo-monoamniotic twins resulting from an original MD twin gestation antenatally detected at the time of FLP for the treatment of TTTS. Fetoscopic findings included a short falciform remnant of the dividing membrane with an irregular margin, indicating that the cause of spontaneous septostomy would be a developmental disturbance or pressure exerted by disproportionate enlargement of one of the two sacs. In addition, although we cannot precisely know the timing of spontaneous septostomy and resulting entanglement, it appears that this occurred midtrimester according to the fetoscopic findings.

The most important concern following antepartum septostomy is cord entanglement, which occurred in 11 out of the 17 reported cases (64%), approximating the reported risk in true monoamniotic twins (70%).[13] Monoamniotic twinning is associated with a per case mortality rate of 54%[14] secondary to prematurity, growth restriction, congenital anomalies, vascular anastomosis and most commonly, umbilical cord entanglement. The perinatal management of this case after FLP was controversial. Pasquini *et al.* reported that sulindac therapy after 20 weeks of gestation, close ultrasound surveillance and elective cesarean section at 32 weeks of gestation following antenatal steroids improved perinatal survival of monoamniotic twins.[15] We managed this case according to this regimen with a successful result.

Most placentas are incompletely examined after birth, and the true incidence of disruption of the dividing-membrane with amniotic plica may be underreported. It is possible that the incidence of true monoamniotic placentation may be even less than 1% of all twins, with many suspected monoamniotic placentas representing disrupted diamniotic-monochorionic placentas. When a 'thin' dividing membrane is visualized at any time during a twin gestation, it is important to remember that rupture of this membrane may subsequently occur. For this reason, a careful inspection of the dividing membrane should be performed at follow-up ultrasound examination. In addition, if a monoamniotic gestation is suspected, the presence of a dividing membrane on previous ultrasound examination cannot rule out the possibility of a dividing membrane rupture with formation of monoamniotic gestation later in pregnancy.

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Original Paper

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Perinatal Outcome of Monochorionic Twins with Selective Intrauterine Growth Restriction and Different Types of Umbilical Artery Doppler under Expectant Management

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Key Words
Monochorionic twins · Selective intrauterine fetal growth restriction · Umbilical artery · Perinatal prognosis

Abstract
Objectives: To evaluate the prognosis of monochorionic twins with selective intrauterine growth restriction (sIUGR), classified according to the type of umbilical artery Doppler, under expectant management. ***Methods:*** The outcome of 81 cases with isolated sIUGR was evaluated according to a classification based on umbilical artery (UA) Doppler diastolic flow in the IUGR twin (I: present, II: constantly absent/reverse, III: intermittently absent/reverse). Selective feticide was not considered due to legal constraints. Perinatal outcomes included perinatal death and neurological outcome at 6 months of age. ***Results:*** From 81 cases with the diagnosis of sIUGR, twin-twin transfusion was diagnosed in 18 cases. This left 63 cases, of which 23 were classified as type I (36.5%), 27 as type II (42.9%) and 13 as type III (20.6%). Intrauterine death occurred in 4.3% (1), 29.6% (8) and 15.4% (2) among IUGR twins, and 4.3% (1), 22.2% (6) and 0.0% (0) among larger twins. Neonatal death occurred in 0.0% (0), 18.5% (5) and 0.0% (0) among IUGR twins, and 0.0% (0), 11.1% (3) and 23.0% (3) among larger twins. Neurological abnormalities at 6 months were found in 4.3% (1), 14.8% (4) and 23.1% (3) in smaller twins and 0.0% (0), 11.1% (3) and 38.5% (5) in larger twins, respectively. Intact survival at 6 months was recorded in 91% (21), 37% (10) and 61% (8) in smaller twins and 95% (22), 55% (15) and 38% (5) in larger twins, respectively. ***Conclusion:*** The outcome in monochorionic twins with sIUGR and abnormal umbilical artery Doppler is poor under expectant management. Normal Doppler seems to be associated with a good prognosis.

Introduction

The incidence of selective intrauterine growth restriction (sIUGR) is approximately 11–14% among monochorionic (MC) twins [1–3], and this condition has been shown to be associated with substantial perinatal risks for both fetuses [1, 3–7]. Uneven placental sharing is thought to be the principal cause of this condition, while the clinical process can depend to some degree on the combination of placental vascular anastomoses [3, 6–8]. Recently, a classification system according to the characteristics of

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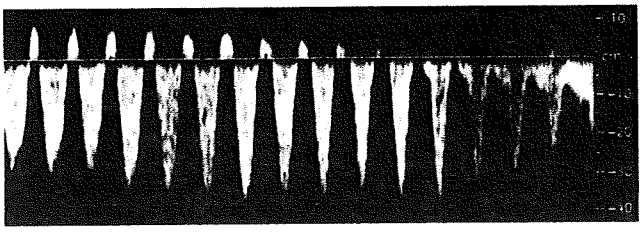

Fig. 1. Typical image of intermittent AREDF in the umbilical artery Doppler waveforms, with cycles intermittently showing AREDF.

diastolic Doppler flow in the umbilical artery (UA) of the smaller twin was advocated by Gratacos et al. [6] to differentiate cases into 3 different clinical forms: type I, normal UA Doppler; type II, persistent absent or reversed end-diastolic velocity flow (AREDF), or type III, intermittent AREDF (iAREDF). While outcomes for type I pregnancies are commonly favorable, IUGR twins in type II cases show in most cases fetal deterioration with a high associated risk of intrauterine fetal death (IUFD) [6]. MC twins with type III sIUGR are characterized by an atypical clinical evolution. About 15% of IUGR twins die unexpectedly and 20% of the larger fetuses show complications of neurological damage due to acute feto-fetal transfusion accidents via arterio-arterial anastomoses [6].

One limitation of previous studies on MC twins with sIUGR is that cord occlusion was performed, either electively [4] or because of fetal deterioration [6]. Therefore, it is unknown whether intervention may have biased the outcome of these clinical series.

In this study, we report the natural history of MC pregnancies complicated with sIUGR in a consecutive series of 81 cases managed expectantly. Perinatal outcome was compared among three study groups established according to the classification system based on the type of UA Doppler in the smaller twin.

Methods

A total of 81 MC twin pregnancies were diagnosed with sIUGR before gestational week 26 in three institutions in Japan from 2001 to 2008. Patients provided informed consent to have their data recorded for clinical studies, which were approved by the Institutional Review Boards at the respective institutions. The definition of sIUGR was an estimated fetal body weight below the 10th percentile in the smaller twin. Twin-twin transfusion syndrome (TTTS) was defined as the presence of ultrasound findings of polyhydramnios in one twin and oligohydramnios in the other, together with markedly discordant bladders, as previously defined [9]. Cases with TTTS or the diagnosis of a fetal malformation at the time of initial diagnosis were not included in this study. Cases with sIUGR were classified into 3 groups based on UA Doppler flow: type I, positive end-diastolic velocity in UA; type II, AREDF constantly observed, or type III, iAREDF defined as the clear observation of abnormal diastolic flow waveforms following an intermittent pattern within a short interval (fig. 1) [6]. Doppler waveforms were recorded using a minimum of three measurements at a free loop in each UA in the absence of fetal or maternal movement. Doppler sampling was performed using a 3.5- or 5-MHz curved array transducer with spatial peak temporal average intensities of <100 mW/cm^2. The angle of insonation was 0° or as close to 0° as possible. The pictures of Doppler exams were available and of good quality from all cases. The diagnosis was established by the characteristics of Doppler at enrolment, but a minimum of two consecutive examinations confirming the initial findings were required at each participating institution.

Fetal condition was monitored by ultrasonography, including fetal growth curves, amniotic pocket and UA Doppler, in combination with fetal heart rate (FHR) monitoring on non-stress test or fetal biophysical profile at these three centers or the referring hospitals. If a case was diagnosed with TTTS before gestational week 26 after the initial diagnosis of sIUGR, laser therapy was contemplated. Selective feticide by cord occlusion was not an option in our clinical setting, and therefore all cases not diagnosed as having TTTS during the observation period were managed expectantly. Indications and route of delivery were decided at the discretion of the attending physicians. Principally, delivery was considered by fetal indications, including fetal deterioration defined by abnormal FHR and/or abnormal biophysical profiling (BPP) score, and by estimated fetal growth arrest at least for 2 weeks after 32 weeks of gestation. Abnormal Doppler waveforms including reversed flow in ductus venosus and reversed flow in umbilical artery were used in some cases, but since the study period was long they were not used consistently for clinical decisions throughout the whole study period.

The occurrence of TTTS was recorded. Perinatal outcome, including the rate of intrauterine and neonatal death, and the rate of neurological morbidity at 6 months of age was recorded in all twins. All neonates were assessed by neonatologists and ultrasonographic brain scan was performed normally and investigation by MRI was indicated when ultrasonography revealed abnormal brain scans within the 6 months' observational period. Any significant abnormal findings on brain ultrasonography or MRI, including intraventricular hemorrhage (grade III or IV), cystic periventricular leukomalacia, blindness, deafness were regarded as neurological morbidity as defined before [9]. The absence of the above mentioned neurological morbidity at 6 months of age was defined as intact survival. Infants were not assessed by any developmental tests in this study.

Results

A total of 81 cases were recorded during the study period, comprising 26 cases of type I, 40 cases of type II and 15 cases of type III. The incidence of TTTS before gestational week 26 after an initial diagnosis of sIUGR was

Table 1. Perinatal outcome according to a classification based on umbilical artery Doppler

	Type I (n = 23)	Type II (n = 27)	Type III (n = 13)
GA at delivery, weeks, median (range)	36 (26–38)	28 (18–40)	31 (25–37)
Fetal indication for delivery, % (n)	30.4 (7)	70.4 (19)	69.2 (9)
Fetal deterioration in smaller twins, % (n)	8.7 (2)	25.9 (7)	15.4 (2)
Growth arrest in smaller twins, % (n)	3 (13.0)	11.1 (3)	7.7 (1)
Fetal deterioration in larger twins, % (n)	4.3 (1)	7.4 (2)	38.5 (5)
Growth arrest in larger twins, % (n)	0.0 (0)	0.0 (0)	0.0 (0)
Fetal deterioration in both twins, % (n)	4.3 (1)	0.0 (0)	7.7 (1)
Intrauterine both fetal demise, % (n)	0.0 (0)	14.8 (4)	0.0 (0)
Miscarriage, % (n)	0.0 (0)	7.4 (2)	0.0 (0)
IUFD of smaller twins, % (n)	4.3 (1)	29.6 (8)	15.4 (2)
IUFD of larger twins, % (n)	4.3 (1)	22.2 (6)	0.0 (0)
NND of smaller twins, % (n)	0.0 (0)	18.5 (5)	0.0 (0)
NND of larger twins, % (n)	0.0 (0)	11.1 (3)	23.1 (3)
NM of smaller twins, % (n)	4.3 (1)	14.8 (4)	23.1 (3)
NM of larger twins, % (n)	0.0 (0)	11.1 (3)	38.5 (5)

GA = Gestational age; IUFD = intrauterine fetal death; NND = neonatal death; NM = neurological morbidity.

11.5% (3/26) in type I, 32.5% (13/40) in type II and 13.3% (2/15) in type III. All 18 patients with TTTS were treated by laser surgery. This left 63 patients with isolated sIUGR, distributed in 23 type I patients, 27 type II patients and 13 type III patients (table 1).

Median gestational age at delivery was 36 weeks (range, 26–38 weeks) in type I, 28 weeks (range, 18–40 weeks) in type II and 31 weeks (range, 25–37 weeks) in type III. The rate of intrauterine death was 4.3% (1), 29.6% (8) and 15.4% (2) in the IUGR twins, and 4.3% (1), 22.2% (6) and 0.0% (0) in the larger twin (table 1). Delivery was indicated for fetal reasons as defined above in 30.4% of type I cases, 70.4% of type II cases, and 69.2% of type III cases. In the remaining patients delivery occurred due to spontaneous labor or it was indicated for maternal reasons.

Data on postnatal evolution are summarized in table 1. The rate of neonatal mortality in types I, II and III was 0.0% (0), 18.5% (5) and 0.0% (0) among smaller twins, and 0.0% (0), 11.1% (3) and 23.0% (3) among larger twins, respectively. There was no infant death after the neonatal period in any of the three study groups. Neurological morbidity within 6 months after birth, as defined above, was found in 4.3% (1), 14.8% (4) and 23.1% (3) of smaller twins and in 0.0% (0), 11.1% (3) and 38.5% (5) of larger twins in pregnancies defined as type I, II and III, respectively.

When the totality of cases with and without intact survival was analyzed, among the 23 type I twins, 91.3% (21) smaller twins and 95.7% (22) larger twins were defined as having intact survival (IS). Among 27 type II pregnancies, 37.0% (10) smaller and 55.6% (15) larger twins had IS. Finally, among 13 type III twins, 61.5% (8) smaller and 38.5% (5) larger infants were defined as having IS. The distribution of cases within each pregnancy type according to the presence of IS in both fetuses, only one or none are displayed in figure 2.

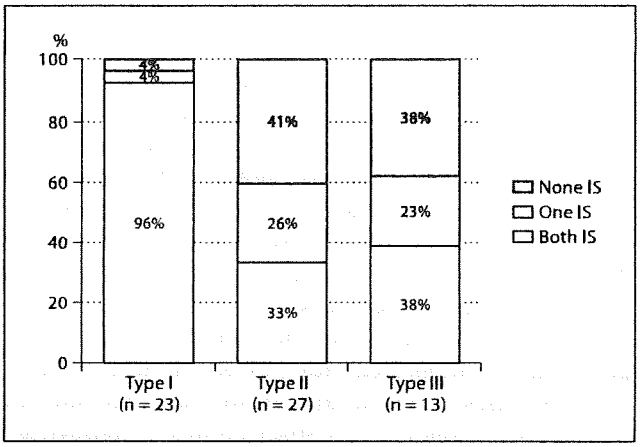

Fig. 2. Pregnancy outcome per mother; the number of infants with intact survival. IS = Intact survival; not IS = death or neurological morbidity.

Discussion

Perinatal prognosis has previously been described for 134 MC twins with sIUGR according to a classification system based on UA Doppler waveforms, with umbilical cord occlusion performed for some cases with abnormal UA based on predicted poor outcome [6]. On the contrary, the present study described perinatal outcomes in a clinical series of cases complicated with sIUGR and managed expectantly with early delivery if warranted, since selective feticide was not applicable due to legal constraints. Among the limitations which must be considered as potential biases in this clinical series is the retrospective nature of the study, and the fact that subjects included patients referred from scattered hospitals, although patients were diagnosed and classified on UA Doppler by specialists at each of the three participating centers. Nevertheless, these results could be of value in clarifying the natural history of twins with sIUGR.

It was noteworthy that the incidence of TTTS before gestational week 26 in the observational period was around one-third in type II cases, while that in type I or III cases was around 12%. This finding could indicate that cases with continuously abnormal UA Doppler in the smaller twin might be at higher risk for TTTS. Type I cases could be relatively protected from TTTS because of a higher number of placental anastomoses, which might allow a more efficient inter-twin blood exchange [3]. Likewise, type III could also be relatively protected from the occurrence of TTTS by the presence of large artery-to-artery anastomoses [6, 10]. Unfortunately, this study did not analyze in detail placental vascular anastomoses preventing any comparison in these respects.

Perinatal outcomes for type I twins were in general favorable, with an intact survival rate in both smaller and larger twins over 90%. The findings are in line with previously reported data [6]. In the light of this evidence, it might seem reasonable that type I patients be managed conservatively until late in gestation. Conversely, type II patients showed the worst prognosis among the three study groups. IS in type II was only 37.0% in smaller twins and 55.6% in larger twins. Of note was the fact that 48.1% of the smaller fetuses showed perinatal death including fetal and neonatal death. Our findings are in line with those of Quintero et al. [4], reporting a high rate of IUFD in type II fetuses managed expectantly. This complication may have remarkable consequences on the outcome of the other twin, due to the risk of acute feto-fetal hemorrhage [11–13]. In a previous report, in utero deterioration of the sIUGR fetus was found in 90.0% of type II [6]. Although in the present study we used a different definition for fetal deterioration, 70% of the type II pregnancies here reported needed delivery due to fetal indications.

The clinical evolution of type III twins presenting with iAREDF has been reported to be atypical. Although sIUGR fetuses differ from type II by failing to show signs of fetal hypoxic deterioration, some sIUGR fetuses may die unexpectedly. More importantly, the proportion of larger twins presenting neurological abnormalities such as PVL may be high in spite of both fetuses being born alive [5, 6]. Only a small number of type III cases were included in the present study. However, the results appear similar to those previously reported [5, 6], with 15.4% of smaller twins presenting IUFD and 38.5% of larger twins showing brain damage.

As the outcome of MC pregnancies with sIUGR and abnormal UA Doppler seems to be clearly unfavorable, some sort of intervention could be considered for these cases at the time of diagnosis. Umbilical cord occlusion for selective feticide has been extensively reported as an option for complicated or discordant MC twins [14, 15], and this procedure could be considered as an option for type II and III pregnancies. However, the use of this technique may be controversial. Selective feticide reduces by definition the survival rate to 50%, and in some cases the remaining twin can also present perinatal death or neurological morbidity [14]. For this reason, and particularly in countries such as Japan where feticide is usually ethically unacceptable, the application of laser coagulation for placental communicating vessels may be an option. The overwhelming advantage that this therapy represents for TTTS [9] has not been reproduced in preliminary clinical series reporting the use of laser placental coagulation in type II [4] or type III cases [4, 16]. Although the number of cases included in these studies has so far been small and further experience may be required, the results suggest that laser may increase the chances of fetal death of the smaller twin, but it might protect the larger twin from the consequences of fetal death of the IUGR fetus [4, 16].

In conclusion, clinical evolution and perinatal outcome with expectant management was different in MC twins with sIUGR classified according to the type of UA Doppler flow in the sIUGR fetus. In general, the outcome in MC twins with sIUGR and abnormal umbilical artery Doppler was markedly poor under expectant management, while normal Doppler seemed to be associated with a good prognosis. Fetal intervention such as cord

occlusion or laser therapy might be considered as a management option for sIUGR cases with abnormal Doppler findings, but the benefit of this options remains to be evaluated in further clinical studies.

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Fetal arrhythmia: Prenatal diagnosis and perinatal management

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Abstract

The importance of managing fetal arrhythmia has increased over the past three decades. Although most fetal arrhythmias are benign, some types cause fetal hydrops and can lead to fetal death. With the aim of improving the outcome in such cases, various studies for prenatal diagnosis and perinatal management have been published. Detailed analysis of the type of arrhythmia *in utero* is possible using M-mode and Doppler echocardiography. In particular, a simultaneous record of Doppler waveform at the superior venous cava and the ascending aorta has become an important and useful method of assessing the interval between atrial and ventricular contractions. Common causes of fetal tachycardia (ventricular heart rate faster than 180 bpm), are paroxysmal supraventricular tachycardia (SVT) with 1:1 atrioventricular (AV) relation and atrial flutter with 2:1 AV relation. Of fetal SVT, short ventriculo-atrial (VA) interval tachycardia due to atrioventricular reentrant tachycardia is more common than long VA interval. Most fetuses with tachycardia are successfully treated *in utero* by transplacental administration of antiarrhythmic drugs. Digoxin is widely accepted as a first-line antiarrhythmic drug. Sotalol, flecainide and amiodarone are used as second-line drugs when digoxin fails to achieve conversion to sinus rhythm. Fetal bradycardia is diagnosed when the fetal ventricular heart rate is slower than 100 bpm, mainly due to AV block. Approximately half of all cases are caused by associated congenital heart disease, and the remaining cases that have normal cardiac structure are often caused by maternal SS-A antibody. The efficacy of prenatal treatment for fetal AV block is limited compared with treatment for fetal tachycardia. Beta stimulants and steroids have been reported as effective transplacental treatments for fetal AV block. Perinatal management based on prospective clinical study protocol rather than individual experience is crucial for further improvement of outcome in fetuses with tachycardia and bradycardia.

Key words: fetal arrhythmia, fetal echocardiography, prenatal diagnosis, prenatal treatment.

The importance of managing fetal arrhythmia has increased over the past three decades. Fetal arrhythmia is often found during fetal heart monitoring or routine prenatal ultrasound examination. Although most fetal arrhythmias are benign, some cause fetal hydrops and can lead to fetal death.[1,2] To improve the outcome in such cases, various studies of prenatal diagnosis and perinatal management have been published. Up-to-date knowledge of effective methods of diagnosing fetal arrhythmia and the selection of appropriate perinatal treatment is crucial for managing affected fetuses. In the present paper, we summarize the current method of prenatal diagnosis and perinatal management of fetal arrhythmia based on recent publications.

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History of Managing Fetal Arrhythmias

Prenatal recognition and treatment of fetal tachycardia began in the 1970s. After the first report of prenatal diagnosis using M-mode echocardiography was published in 1980 by Kleinman *et al.*,[3] many reports of prenatal treatment of fetal tachycardia using various types of antiarrhythmic drugs were published in the 1980s. In the 1990s, researchers were more focused on refractory cases.[4–6] To enable a more detailed prenatal diagnosis, measurement of the ventriculo-atrial (VA) interval was reported in 1998,[7] and the magnetocardiogram was introduced as a useful modality.[8] In the 21st century, researches began to focus on better strategies to manage fetal arrhythmia by conducting multicenter trials with larger numbers of patients.[9]

Definition and Method of Prenatal Diagnosis

There are three types of fetal arrhythmias.[1,2] The most common form is irregular heartbeat, mainly caused by ectopic beats. When the ventricular rate is faster than 180 bpm or slower than 100 bpm, such fetal arrhythmia is classified as fetal tachycardia or fetal bradycardia, respectively. Detailed analysis of the type of arrhythmia *in utero* is possible using M-mode and Doppler echocardiography.

M-mode echocardiography

An M-mode trace of ventricular and atrial motion demonstrates cardiac rhythm and rate. A simultaneous record of both ventricular and atrial contractions with a four-chamber view is especially useful for assessing the relation of atrioventricular (AV) mechanical connection in fetuses with arrhythmias, and can determine the mechanism causing the fetal arrhythmia (Figs 1,2).[1,2]

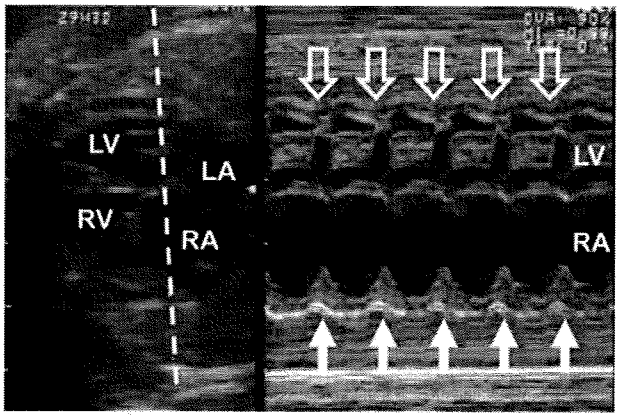

Figure 1 Simultaneous M-mode recording of both ventricles and atria. M-mode recording in a fetus with supraventricular tachycardia reveals 1:1 relation of atrial (closed arrow) and ventricular contraction (open arrow) with a ventricular rate of 210 bpm. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

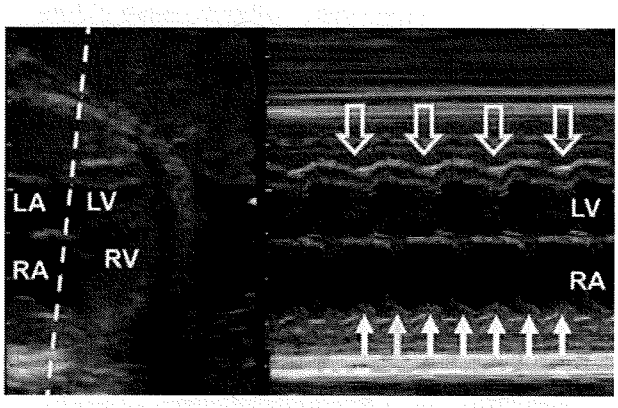

Figure 2 M-mode recording in a fetus with atrial flutter and 2:1 atrioventricular conduction, with an atrial (closed arrow) rate of 510 bpm and a ventricular (open arrow) rate of 255 bpm. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

Doppler echocardiography

Recently, a simultaneous record of Doppler waveforms at the superior venous cava (SVC) and the ascending aorta (aAo) was introduced as a useful method of assessing cardiac arrhythmias (Fig. 3).[10,11] The beginning of reverse flow at the SVC created by atrial contraction and the beginning of forward flow at the aAo created by ventricular contraction are interpreted as the beginning of P and QRS wave by electrocardiogram (ECG), respectively. Using Doppler waveform, the relation and time intervals of the atrial and ventricular contractions can be measured.[12,13] The pulmonary vein and the pulmonary artery,[14] or the innominate vein and the aortic arch can also be used as alternative methods of assessing simultaneous venous and arterial waveforms.[12]

Another method of measuring AV conduction time interval is the simultaneous record of left ventricular inflow and outflow waveforms.[2] Although this method is relatively easy, AV contraction relation cannot be assessed once the tachycardia begins because E wave, first peak, and A wave, second peak of the inflow pattern cannot be distinguished in this condition.

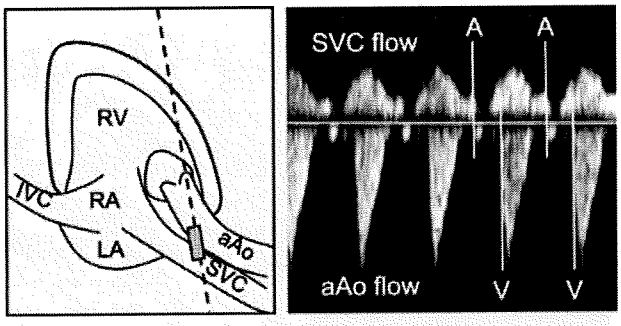

Figure 3 Simultaneous Doppler trace of the ascending aorta (aAo) and the superior vena cava (SVC). Beginning of reverse flow at SVC (A) and forward flow at aAo (V) represent the timing of atrial and ventricular contraction, respectively. IVC, inferior vena cava; LA, left atrium; RA, right atrium; RV, right ventricle.

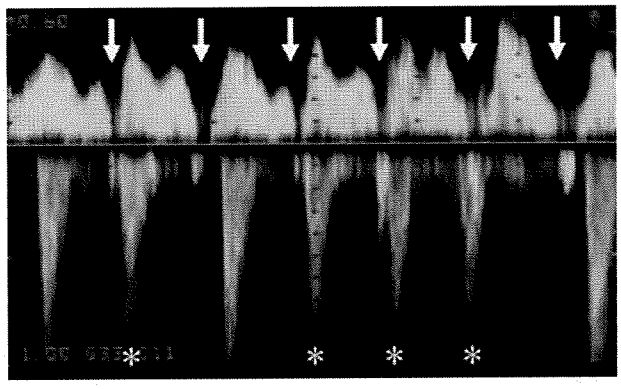

Figure 4 Simultaneous Doppler trace of the ascending aorta and the superior vena cava in a fetus with ventricular or junctional tachycardia reveals regular atrial contraction with reversal flow at the superior vena cava (arrows) and faster ventricular contraction (asterisk).

Simple measurement of the time length of A wave may be another method to screen the prolongation of AV interval.

Tissue Doppler echocardiography, which can demonstrate detail timing of myocardial contraction, is a useful tool for evaluating fetal arrhythmia.[13,15] Because the tissue Doppler method has become available in the equipment used currently, this technique may become part of routine examination in the near future to diagnose fetal arrhythmias.

Tachycardia

Prenatal diagnosis

Fetal tachycardia is diagnosed when the fetal ventricular heart rate is faster than 180 bpm.[1,2,11] Common causes of fetal tachycardia are paroxysmal supraventricular tachycardia (PSVT) and atrial flutter (AFL). There are other rare types of fetal arrhythmias, such as ventricular tachycardia (VT), junctional tachycardia, and multiforcal atrial tachycardia (MAT). Fetal tachycardia is classified based on the relation of the AV contraction observed by fetal echocardiography. Fetal PSVT has a 1:1 AV relation (Fig. 1). Fetal AFL has a very fast atrial heart rate, such as 400 or 500 bpm, and 2:1 (occasionally 3:1 or 4:1) AV relation (Fig. 2). Fetal VT has ventricular tachycardia with dissociated atrial contraction (Fig. 4). Fetal MAT shows irregular atrial tachycardia and ventricular contraction. Although tachycardia is sometimes intermittent during prenatal examination, the chance of hemodynamic complications and development of fetal hydrops remain high.

PSVT in most fetuses is caused by atrioventricular reentrant tachycardia (AVRT) due to Wolff–Parkinson–White syndrome.[8,11] Both the atrial and ventricular heart rates range from 200–300 bpm (Fig. 1). Measurement of the time interval from the ventricular contraction to the following atrial contraction (VA interval) by Doppler echocardiography reveals a short VA interval (Fig. 5).[10,11] The measurement of this VA interval is very useful to distinguish AVRT (short VA interval) from other types of fetal tachycardias, such as atrioventricular nodal reentrant tachycardia (AVNRT) and permanent junctional reciprocating tachycardia (PJRT), which demonstrates a long VA interval (Fig. 6).

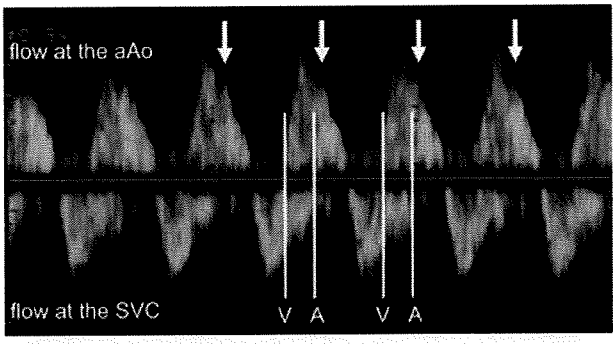

Figure 5 Simultaneous Doppler trace of the ascending aorta (aAo) and the superior vena cava (SVC) in a fetus with supraventricular tachycardia with short ventriculo-atrial interval. Although high-velocity reversal flows of SVC is almost over-wrapped to the flow of aAo, the starting point of the reversal flow can be detected from the interrupted forward flow of SVC.

Perinatal management

Most fetuses with both PSVT and AFL are successfully treated *in utero* by transplacental administration of

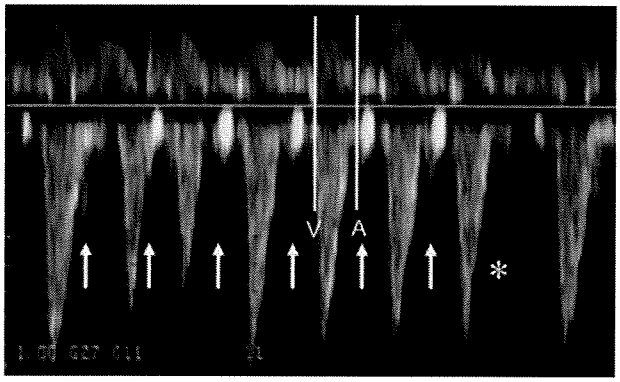

Figure 6 Simultaneous Doppler trace of the ascending aorta and the superior vena cava in a fetus with 1:1 atrioventricular conducted tachycardia with long ventriculo-atrial interval. Tachycardic atrial contraction (A, arrows) disappears after the seventh ventricular contraction (asterisk), and the tachycardia is stopped.

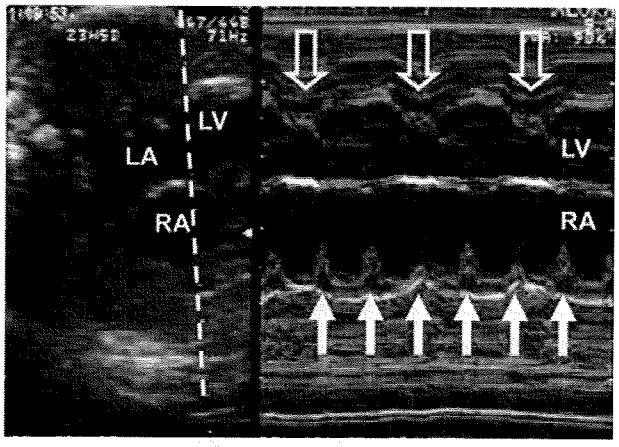

Figure 7 Simultaneous M-mode recording of both ventricles and atria in a fetus with complete atrioventricular block reveals complete dissociation of atrial and ventricular contraction with a ventricular rate of 65 bpm. Large arrows, ventricular contractions; small arrows, atrial contractions; LA, left atrium; LV, left ventricle; RA, right atrium.

antiarrhythmic drugs.[6,9,10,11] Digoxin is widely accepted as a first-line antiarrhythmic drug. Sotalol, flecainide and amiodarone are used as second-line drugs when digoxin fails to achieve conversion to sinus rhythm.[16–21] For fetuses with hydrops and fetal PSVT with long VA interval, digoxin is rarely effective.[11] For fetuses with hydrops, the placental transfer of the digoxin is limited. Hence, sotalol or flecainide, which have good placental transfer ability, should be used from the beginning of fetal treatment for hydrops. Fetal intramuscular administration of digoxin with maternal administration of amiodarone is another effective method.[21]

Although intrauterine treatment is very effective in fetuses with tachycardia, treatment after delivery is also very effective. Hence, decisions for which cases are treated *in utero* or postnatally is often difficult. Management of a premature neonate under hemodynamically unstable conditions with tachycardia and decreased cardiac function is difficult.[22] Hence, it is important not to select postnatal treatment too quickly in premature gestation, even when the fetus has already developed hydrops. Once the tachycardia is converted to sinus rhythm, the hydrops will recover and the fetus can be delivered at term by vaginal birth. However, when the hydrops continues for more than 2 weeks without conversion of tachycardia, postnatal treatment is recommended.

It is difficult to predict when the fetus will develop hydrops.[23,24] Several Doppler echocardiographic parameters that demonstrate congestive heart failure cannot be used at this extremely high heart rate. Serial measurement of the cardiothoracic ratio may be useful for monitoring the degree of heart failure. The presence of atrioventricular valve regurgitation, especially at the mitral valve, may represent severe congestive heart failure.

The safety of the mother is of great concern when managing fetal tachycardia. Administration of antiarrhythmic drugs for intrauterine treatment may cause pro-arrhythmia and threaten the mother. ECG monitoring, especially of the QT prolongation of the mother is very important when a new drug is started or the dosage is increased.

Bradycardia

Prenatal diagnosis

Fetal bradycardia is diagnosed when the fetal ventricular heart rate is slower than 100 bpm, mainly due to AV block (Fig. 7).[1,11,25] Approximately half of all cases are caused by associated congenital heart disease (CHD), and the remaining cases that have normal cardiac structure are often caused by maternal SS-A antibody.[26–28] The two most common CHD associated with AV block are left atrial isomerism (Fig. 8) and discordant AV connection. Maternal SS-A antibody to AV block is usually that for 52kd SS-A, and many mothers are rarely diagnosed with collagen disease when the fetus develops AV block.[29–32] Although rare, the other important cause of fetal bradycardia is long QT syndrome, which can cause 2:1 AV block or sinus

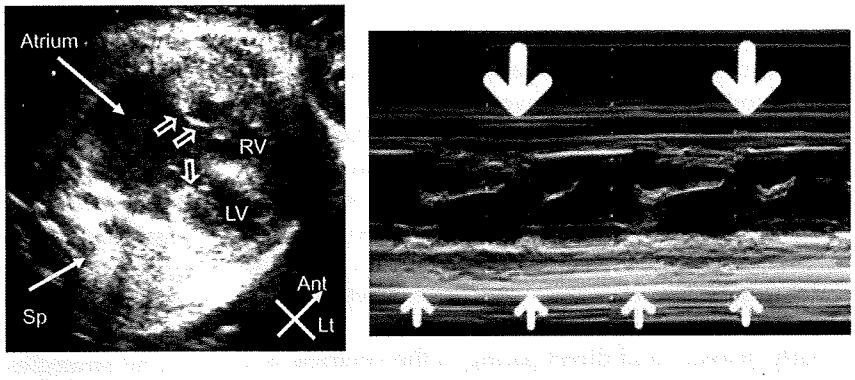

Figure 8 Left panel reveals four-chamber view of polysplenia with the single atrium, the common atrioventricular valve (open arrows) and cardiomegaly. Right panel reveals simultaneous M-mode recording of ventricles (large arrows) and atria (small arrows) in this case, which demonstrates 2:1 atrioventricular block. Ant, anterior; Lt, left; LV, left ventricle; RV, right ventricle; Sp, spine.

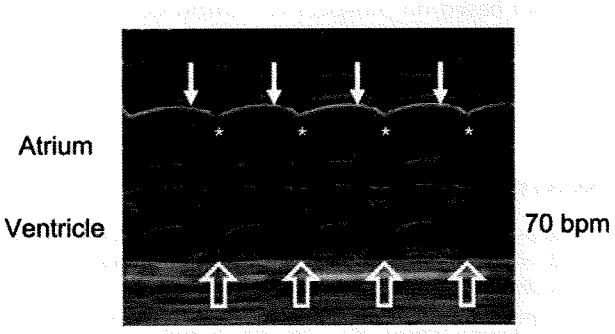

Figure 9 Simultaneous M-mode recording of ventricles and atria in a fetus with blocked paroxysmal atrial contraction (PAC) with bigeminy. The PAC (asterisk) shortly after regular atrial conduction (small arrows) does not conduct to the ventricle causing bradycardia with a ventricular rate of 70 bpm.

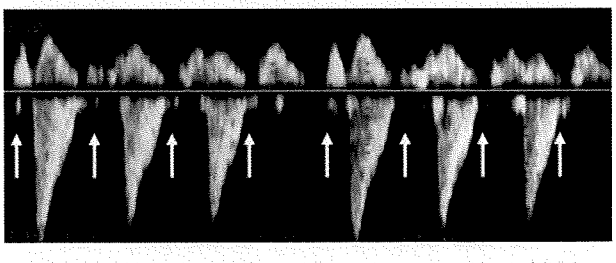

Figure 10 Wenckebach type atrioventricular block. Simultaneous Doppler trace of the ascending aorta and the superior vena cava reveals atrial contraction with regular rhythm (arrows), atrioventricular conducting time of gradual prolongation, and block with pose of ventricular contraction.

bradycardia.[33] Blocked paroxysmal atrial contraction (PAC) with bigeminy also mimics 2:1 AV block and causes fetal bradycardia (Fig. 9).[11]

Doppler echocardiography is useful for diagnosing fetal bradycardia. The relation and interval of atrial and ventricular contractions revealed by SVC and aAo Doppler flow can demonstrate the severity of AV block, not only complete dissociation of AV contraction, but also first-degree and Wenckebach-type second-degree AV block (Fig. 10).[11,34]

Fetal bradycardia with either CHD or fetal hydrops has a significantly worse prognosis.[26,27] Although a heart rate of less than 55 bpm is thought to be the cut-line for congestive heart failure, some recent reports included cases without heart failure even when the fetal heart rate was less than 50 bpm.[27] Cardiac function or presence of CHD affects the severity of congestive heart failure.[35] It is important that transferred maternal IgG can cause pleural, pericardial and peritoneal effusion, in addition to myocarditis and poor cardiac function in the fetus, even if there is no hydrops.[36]

Perinatal management

Efficacy of prenatal treatment for fetal AV block is limited compared with treatment for fetal tachycardia. Beta stimulants and steroids have been reported to be effective transplacental treatments for fetal AV block.[11,37,38] Beta stimulants, such as ritodrine, terbutaline, and salbutamol effectively increase fetal ventricular rate by approximately 10–20% and reverse hydrops in some fetuses with AV block. Several reports have demonstrated that transplacental administration of steroids, such as dexamethasone and betamethasone, are effective for fetuses with AV block caused by anti-SSA antibody.[39–41] Jaeggi *et al.* recently reported that prenatal steroid treatment improves the outcome of fetuses with AV block.[32]

There are two targets for prenatal steroid therapy. The most attractive target is the direct effect of treating AV block. The prompt administration of steroids immediately after the onset of AV block has improved the degree of AV block.[39] However, other studies have shown spontaneous improvement of the degree of AV block without any steroid therapy.[42] Hence, the direct effect of steroids for AV block remains uncertain.