図 2. 胃泡の位置の grade 別頻度

全体の 34.9%に胃泡の右胸腔内脱出を認めた。特に肝脱出例で頻度が高い。

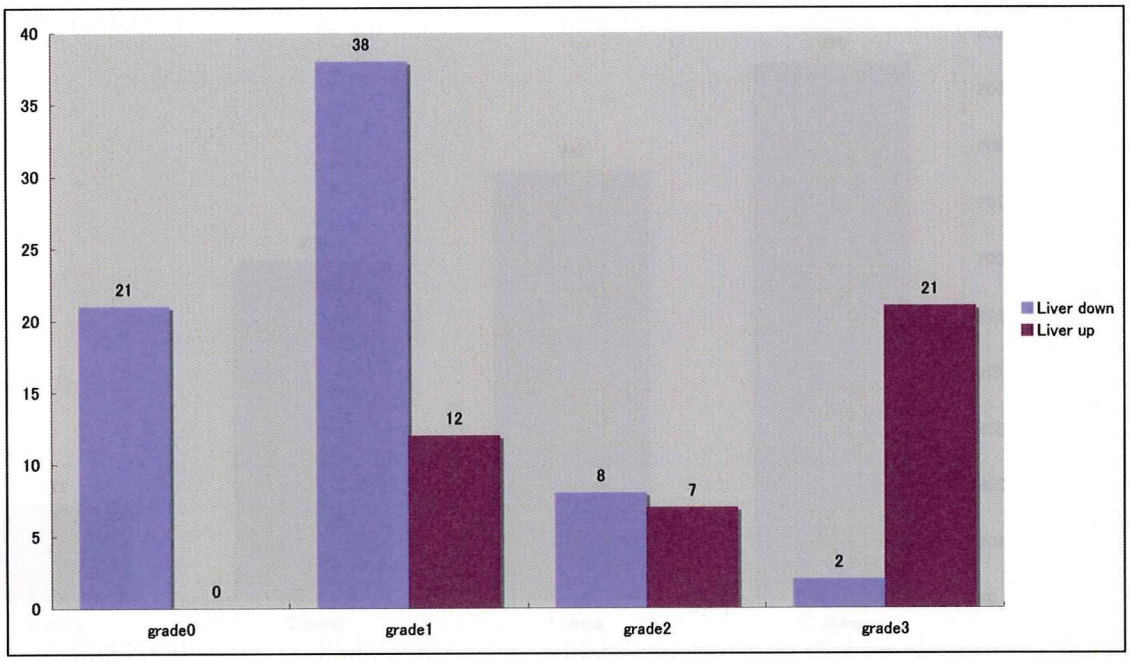


図 3. 胃泡の位置別の合併症なき退院率

Cochran-Armitage trend test において $p<0.0001$

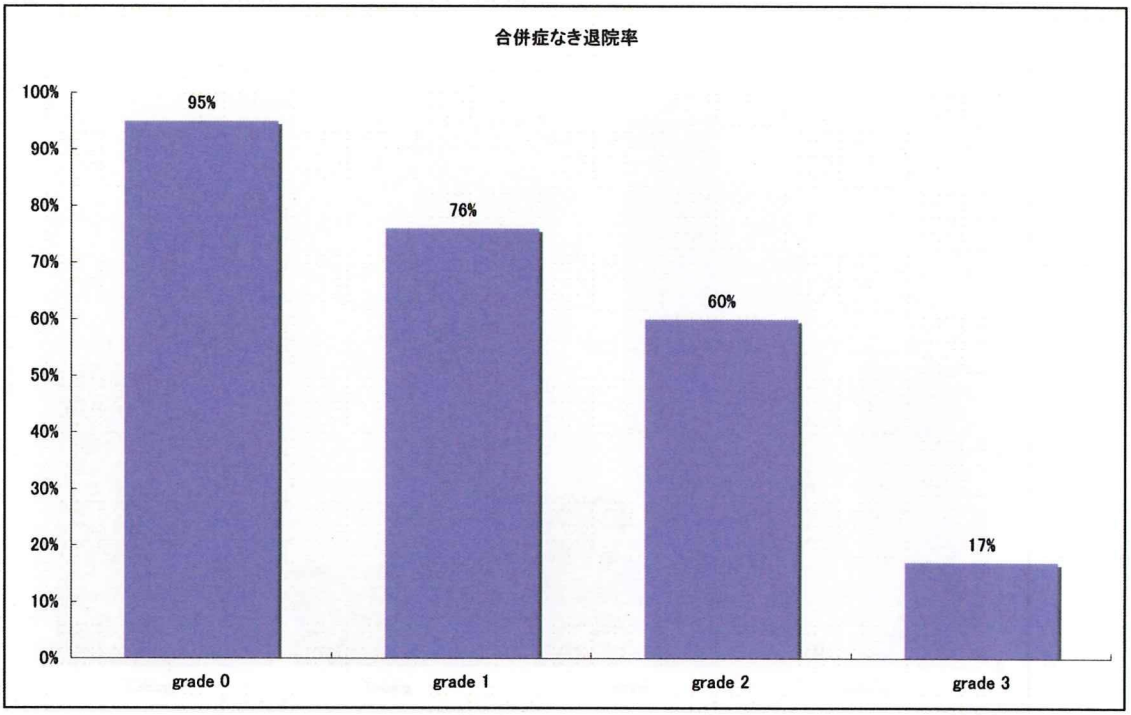
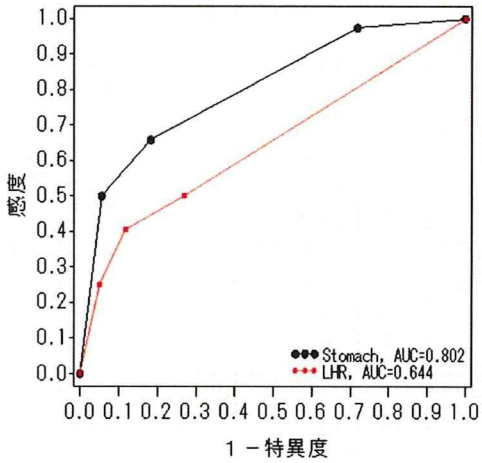


図 4.

LHRのカテゴリ 0～1未満，1～1.2未満，1.2～1.4未満、1.4以上



D. 考察

本症と出生前診断された胎児に理想的な生後治療行った際の自然歴は、今後胎児治療を検討するに当たって必要不可欠な情報である。本研究では母体搬送、治療施設での分娩、出生直後からの gentle ventilation を含めた集中治療を理想的な生後治療と考え、本症の予後に関する横断的調査研究を日本ではじめて実施した。プロトコールを作成し、臨床試験に準じた症例調査票を用い、データマネージメント、統計家による統計処理を行った。調査施設は 5 施設に限定し、データの信頼性が高く精度の高い研究を目指した。

第一の目的は、日本の主要施設で実施されている生後治療の成績評価である。低侵襲化が進んでいるとはいえ、胎児治療には母体に対するリスクが存在する。生後治療に改善の余地が残されているなら、まずそちらの改善を試みることが要求される。第二の目的は、出生前評価によって理想的な生後治療を行っても生命的・機能的予後が不良である一群を選別できるかどうかである。

結果として、最近 6 年間の 117 例を集計することができた。全体の治療成績については奥山からの報告で詳細に検討され、本研究の第一の目的が達成された。今後両親に対して提供する貴重なデータとなるだろう。

出生前に容易に測定可能な諸項目の検討の結果、肝脱出の有無と並んで胃の右胸腔内脱出の有無が重要な予後因子であることが判明した。これは世界的にみても新しい知見である。健側肺の大きさを画像で評価するには熟練を要し、測定誤差が大きく、カットオフ値の設定が難しい、などの欠点がある。それに対して胃泡の位置判定は容易でどの施設でも可能であり、今後普及する可能性が高い。

肝脱出例のなかでも胃の高度右胸腔内脱出を伴う症例の予後は、合併症なき退院率が 9.5%で、現在の理想的な治療を持ってしても極めて厳しい。少数ながら、この一群に対しては胎児治療が検討されてもコンセンサスが得られるものと考えられた。

E. 結論

胎児左横隔膜ヘルニアでは胃の右胸腔内脱出がまれでない。胃泡の位置は肝脱出の有無と並んで重要な予後因子である。胃泡の位置によって肝脱出例の予後をさらに細分化することが可能である。

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H．知的所有権の出願登録状況

なし

Ⅲ. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

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Ⅳ. 研究成果の刊行物・別刷

Fetal Diagnosis and Therapy

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Ultrasound Assessment prior to Laser Photocoagulation for Twin-Twin Transfusion Syndrome for Predicting Intrauterine Fetal Demise after Surgery in Japanese Patients

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Key Words
Twin-twin transfusion syndrome · Ultrasound · Doppler velocimetry · Fetal therapy · Laser therapy · SLPCV

Abstract
Objective: To evaluate the use of ultrasound before selective laser photocoagulation of communicating vessels (SLPCV) for twin–twin transfusion syndrome in predicting intrauterine fetal demise (IUFD). ***Methods:*** Fifty-five patients underwent SLPCV in Japan. Fetal biometry and Doppler studies of the umbilical artery, ductus venosus, and umbilical vein were performed prior to SLPCV. The visualization of the bladder and hydrops was recorded. Association between the parameters and IUFD was analyzed using multiple logistic regression analysis. The study was approved by the Institutional Review Board and patients gave their informed consent. ***Results:*** The IUFD incidence was 25.5% (14/55) in the donors and 12.7% (7/55) in the recipients. Twelve donors and 4 recipients of them ended in unexplainable IUFD. In the analysis of 53 donors, absent or reversed end-diastolic flow of umbilical artery (UAAREDF) was only associated with IUFD ($p = 0.016$). No parameters could predict IUFD in 52 recipients. ***Conclusions:*** UAAREDF may be useful for predicting IUFD of the donor after SLPCV.

Introduction

Twin–twin transfusion syndrome (TTTS) develops in approximately 10% of monochorionic twin pregnancies and is associated with high mortality rates [1, 2]. The anatomical basis for this syndrome may be the existence of intertwin placental vascular anastomoses [3, 4]. The establishment of unbalanced blood flow from the donor twin to the recipient twin through the communicating vessels can result in profound hemodynamic disturbances in each twin. Consequently, the donor twin becomes hypovolemic, leading to oligohydramnios, whereas the recipient twin becomes hypervolemic and develops polyhydramnios and hydrops.

Recently, several favorable outcomes have been reported in which fetoscopic laser photocoagulation of placental communicating vessels has been used for treating TTTS [5–8]. The fetal survival rates were significantly higher in patients subjected to laser treatment than in those treated by serial amniodrainage. Furthermore, the incidences of abnormal neonatal brain scans were also lower in the group treated by selective laser photocoagulation of communicating vessels (SLPCV). Nonetheless, intrauterine fetal demise (IUFD) after laser surgery did occur in at least 23.2% of the fetuses [7–10]. Preoperative ultrasound

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assessment was performed and these parameters were believed to reflect the condition of each fetus immediately prior to surgery; this condition may occasionally be related to the outcome of surgery. The aim of this study was to evaluate the use of ultrasound assessment prior to SLPCV for TTTS in predicting IUFD after surgery.

Methods

Fifty-five Japanese women were diagnosed with TTTS and underwent SLPCV between July 2002 and February 2005. The four Japanese institutions that participated in the Japan Fetoscopy Group are as follows: Seirei Hamamatsu General Hospital, National Center for Child Health and Development, Yamaguchi University Hospital, and Niigata University Graduate School of Medical and Dental Sciences. TTTS was diagnosed on the basis of standard diagnostic criteria: presence of a polyhydramnios amniotic pocket >8 cm in the recipient twin, oligohydramnios amniotic pocket <2 cm in the donor twin, single placenta, thin dividing membrane, and similar external genitalia. All patients met the following criteria for SLPCV: (1) the gestational age was less than 26 weeks (median: 21; range: 16.25) and (2) on the basis of the Quintero staging system, they were in either stage II, III, or IV; stage II, 6 cases; stage III, 37 cases; and stage IV, 12 cases [11]. The surgical procedure of SLPCV was performed by a previously reported method [12, 13]. Patients gave their written consent after intensive counseling, and the study was approved by the ethical committee of each institution.

Routine preoperative ultrasound assessment was performed including fetal biometry and estimation of the amniotic fluid volume, placental location, and umbilical cord insertion. This was followed by color and pulsed Doppler examination within 24 h prior to the surgery. The presence or absence of the fetal bladder in donors was assessed sonographically and the presence or absence of fetal hydropic signs such as ascites, pleural effusions, and skin edema in recipients was documented. The discordant rate (DR) of the estimated fetal weight was calculated as (A-B/A)·100, where A is the estimated fetal weight of the larger twin and B is that of the smaller twin. Doppler samplings were performed using a 3.5-MHz or 5-MHz curved array transducer with spatial peak temporal average intensities of less than 100 mW/cm^2. The high-pass filter was set at the lowest level. In the Doppler studies, the occurrence of absent or reversed end diastolic blood flow velocity in the umbilical artery (UAAREDF), absent or reversed blood flow during atrial contraction in the ductus venosus (DVARF), and pulsatile umbilical venous flow (PUVF) was regarded as critically abnormal. Flow velocity waveforms were recorded during the absence of fetal breathing and/or movements. Umbilical arterial and venous waveforms were recorded from a free loop of the umbilical cord or at the placental cord insertion site. The sample volume for the ductus venosus (DV) was determined from its inlet portion at the umbilical vein (UV).

The study outcome was IUFD after SLPCV. The interval from the procedure to the occurrence of IUFD was noted. If there was an obvious explanation for IUFD such as miscarriage following preterm PROM and umbilical cord entanglement, it was described and excluded in the statistical analysis.

Multiple logistic regression analysis was used to analyze the following ultrasound factors in relation to IUFD after SLPCV: the absence of bladder filling, UAAREDF, DVARF, PUVF, and DR in the donor twins and the occurrence of hydrops fetalis, UAAREDF, DVARF, PUVF, and DR in the recipient twins. Data management and statistical computations were performed with the SPSS v 12.0 (Chicago, Ill., USA) software. The p value for this analysis was set at <0.05.

Results

Sonographic measurements were obtained and complete surgical procedures were performed in all 55 cases. All the patients had already delivered, and the median gestational age at the time of delivery was 31 (range: 21.38) weeks. Recurrence of polyhydramnios after surgery was not observed, and elective abortion after SLPCV was not selected in these cases. Of the 55 pregnancies, both fetuses survived to live-birth in 39 (70.9%), only one fetus survived in 12 (21.8%), and both fetuses died in utero in 4 (7.3%). In one of these 4 cases, the reason for both IUFD could not be explained. Hence, the rate of at least one fetus surviving to live-birth was 92.7% (52/55).

IUFD of the donor twin occurred in 25.5% (14/55) of the patients; the data are shown in table 1. One donor fetus died due to umbilical cord entanglement following iatrogenic perforation of the dividing membrane between twins by laser coagulation. The miscarriage of another donor fetus occurred due to premature rupture of the membrane immediately after the surgery. With the exception of these 2 cases, there was no explanation for the cause of IUFD in 12 cases. IUFD in 11 of these 12 donors occurred within 3 days of SLPCV. Preoperative sonogram confirmed the absence of bladder filling in 58.3% (7/12) of the donors with IUFD, while it was 85.3% (35/41) in the case of live-birth donors. UAAREDF was noted in 91.7% (11/12) of the donors in the IUFD group and in 29.3% (12/41) of those in the live-birth group. DVARF and PUVF were detected in 25.0% (3/12) and 8.3% (1/12) of the donors in the IUFD group and in 0.0% (0/41) and 4.9% (2/41) of those in the live-birth group, respectively. The median (range) of DR in the IUFD group was 39.9% (14.8–49.7), while it was 34.4% (0.0–60.9) in the live-birth group. Multivariate analysis in terms of the above-mentioned ultrasound factors related to donor twins, using multiple logistic regression analysis, showed a significant correlation between UAAREDF and IUFD in donor twins ($p = 0.016$; odds ratio = 18.9; 95% confidence interval = 1.8–204.9) (table 2).

Table 1. Data of cases with IUFD of donor twins

No.	Stage	GA	Bladder	UAAREDF	DVARF	UVPF	DR, %	Day of IUFD
1	IIIa	24	visible	yes	no	no	14.8	1
2	IIIa	24	visible	yes	no	no	45.3	1
3	III	19	invisible	yes	no	no	40.9	1
4	IIIa	20	visible	yes	no	yes	33.3	3
5	IV	23	invisible	yes	yes	no	43.9	1
6	IIIa	19	visible	yes	no	no	40.0	1
7	III	19	invisible	yes	no	no	23.9	1
8	III	24	invisible	yes	no	no	33.4	1
9	III	19	invisible	yes	yes	no	49.4	12
10	IV	17	invisible	yes	no	no	49.7	2
11	III	25	invisible	no	no	no	39.8	1
12	IIIa	23	visible	yes	yes	no	33.3	1
13	IV	20	invisible	no	no	no	21.2	26[a]
14	III	21	invisible	no	no	yes	35.8	0[b]

[a] IUFD due to umbilical cord entanglement following perforation of the dividing membrane by laser.
[b] Miscarriage due to premature rupture of the membrane immediately after surgery.
Day of IUFD = Interval from surgery to IUFD; DR = fetal weight discordant rate; DVARF = absent or reversed blood flow during atrial contraction in the ductus venosus; GA = gestational age at procedure; IIIa = stage III atypical; Stage = Quintero classification for twin–twin transfusion syndrome; UAAREDF = absent or reversed end diastolic flow in the umbilical artery; UVPF = umbilical venous pulsatile flow.

Table 2. Multiple logistic regression analysis of IUFD after surgery on preoperative abnormal ultrasound parameters in donor twins

	IUFD (n = 12)	Live-birth (n = 41)	
Absence of bladder	7 (58.5%)	35 (85.3%)	NS
UAAREDF	11 (91.7%)	12 (29.3%)	p = 0.016*
DVARF	3 (25.0%)	0 (0.0%)	NS
UVPF	1 (8.3%)	2 (4.9%)	NS
DR, % median [range]	39.9 [14.8–49.7]	34.4 [0.0–60.9]	NS

* Odds ratio = 18.9; 95% CI = 1.75–204.9.
DR = Fetal weight discordant rate; DVARF = absent or reversed blood flow during atrial contraction in the ductus venosus; NS = not significant; UAAREDF = absent or reversed end diastolic flow in the umbilical artery; UVPF = umbilical venous pulsatile flow.

In recipient twins, 7 of 55 fetuses (12.7%) resulted in IUFD after SLPCV (table 3). Two recipient twins died due to umbilical cord entanglement following iatrogenic perforation of the dividing membrane and 1 ended in miscarriage caused by premature rupture of the membrane immediately after surgery. Unexplained IUFD occurred in another 4 fetuses within 2 days of the surgery. In these 4 recipient twins with IUFD, hydrops fetalis was noted in 3 (75.0%), while it was observed in 9 of the 48 surviving recipient twins (18.8%). UAAREDF was noted in 0.0% (0/14) of the patients in the IUFD group and in 2.1% (1/48) of those in the surviving group. DVARF and PUVF were observed in 50.0% (2/4) and 50.0% (2/4) of the recipients with IUFD and in 33.3% (16/48) and 60.4% (29/48) of the patients in the live-birth group, respectively. The median (range) of DR in the IUFD group was 33.4% (33.3–40.1), while that of the surviving group was 36.6% (0.0–60.9). Multiple logistic regression analysis of

Table 3. Data on cases with IUFD of recipient twins

No.	Stage	GA	Hydrops	UAAREDF	DVARF	UVPF	DR, %	Day of IUFD
1	IV	25	yes	no	yes	yes	40.1	1
2	IV	21	yes	no	yes	yes	39.8	2
3	IIIa	23	no	no	no	no	33.3	1
4	IV	20	yes	no	no	no	21.2	2
5	III	25	no	no	yes	yes	36.0	27[a]
6	III	19	no	no	no	yes	40.9	58[a]
7	III	21	no	no	no	yes	35.8	0[b]

[a] IUFD due to umbilical cord entanglement following perforation of the dividing membrane.
[b] Miscarriage due to premature rupture of the membrane immediately after surgery.
Day of IUFD = Interval from surgery to IUFD; DR = fetal weight discordant rate; DVARF = absent or reversed blood flow during atrial contraction in the ductus venosus; GA = gestational age at procedure; IIIa = stage III atypical; Stage = Quintero classification for twin–twin transfusion syndrome; UAAREDF = absent or reversed end diastolic flow in the umbilical artery; UVPF = umbilical venous pulsatile flow.

Table 4. Multiple logistic regression analysis of IUFD after surgery on preoperative abnormal ultrasound parameters in recipient twins

	IUFD (n = 4)	Live-birth (n = 48)	
Hydrops fetalis	3 (75.0%)	9 (18.8%)	NS
UAAREDF	0 (0.0%)	1 (2.1%)	NS
DVARF	2 (50.0%)	16 (33.3%)	NS
UVPF	2 (50.0%)	29 (60.4%)	NS
DR, % median [range]	33.4 [33.3–40.1]	36.6 [0.0–60.9]	NS

DR = Fetal weight discordant rate; DVARF = absent or reversed blood flow during atrial contraction in the ductus venosus; NS = not significant; UAAREDF = absent or reversed end diastolic flow in the umbilical artery; UVPF = umbilical venous pulsatile flow.

the above factors related to recipient twins revealed no significant association of IUFD in the case of recipient twins (table 4).

Discussion

SLPCV has resulted in a favorable perinatal outcome in patients with TTTS, when all fetuses could not have been rescued. At present, there exists a possibility that affected fetuses undergoing SLPCV may die in utero. In reports on the outcomes of laser surgery for TTTS, the frequency of IUFD in donors was higher in the case of recipient twins [5–10]. Our data, in which 22.6% of the 53 donors and 8.3% of the 52 recipients ended in unexplainable fetal demise, appear to agree with these findings. In particular, the incidence of unexplained IUFD in donors was higher than in recipients (Fisher's exact probability test, p = 0.030); severe placental insufficiency of the donor twins due to unequal placental sharing might be related to fetal death [9, 10, 14]. Unexplained double fetal demise occurred in only one case. Fourteen surviving co-twins after single fetal death resulted in live-birth though their neurological condition had not been analyzed in this study. These results may imply the extent of the ability of laser surgery in IUFD at this stage, while laser surgery has a protective effect to the death of co-twin after one fetal death has occurred. It is noteworthy that unexplained IUFD occurred in 10 of the 11 donor twins (90.9%) and in all 4 recipient twins (100.0%) within a few days of the surgery. This might be due to the effect of surgery, as inferred before [10]. Obliteration of the

placental vascular anastomoses was confirmed by air injection test in these cases except for the cases with fetal demise whose placenta could not be evaluated because of massive placental infarction.

Detailed analyses by ultrasound, including ordinary Doppler examinations for each fetus with TTTS, should be performed prior to laser surgery. Multiple regression analysis on preoperative sonographic parameters for donor twins revealed a significant correlation between UAAREDF and IUFD after SLPCV. UAAREDF was detected in 23 of the 53 donors prior to surgery (43.4%), and 11 of the 23 (47.8%) resulted in IUFD. This abnormal finding may be considered to be the result of maldevelopment of the placenta and/or uneven placental distribution between each twin. UAAREDF in donors has been regarded as an important prognostic factor for IUFD in cases treated with laser surgery. Ville et al. [5] described UAAREDF as a risk factor for perinatal death of donors after laser surgery in 132 cases treated by laser. Zikulnig et al. [9] reported a lower survival rate of donors with UAAREDF in 121 cases treated by laser surgery without significant difference among these cases. While both studies included the neonatal outcome, Martinez et al. [10] reported that UAAREDF prior to surgery could predict IUFD of donor twins.

In contrast, live-birth after SLPCV occurred in 12 of the 23 donors (52.2%) who had UAAREDF preoperatively, although postoperative Doppler data could not be obtained in this analysis. Even if donor twins show absent or reversed flow in the UA prior to surgery, it is possible that half of them could survive after surgery. UAAREDF of the donors appears to reflect not only the placental insufficiency, but also the fetal hypotension secondary to hemodynamic imbalance. Previous studies have shown that some of the donors with AREDF preoperatively showed reappearance of end-diastolic flow and a decrease in the Pulsatility Index values in the UA after the procedure. This phenomenon could be due to a change in the hemodynamic situation and an increase in the blood volume [9, 10]. This explanation is indirectly supported by the increase in the umbilical venous blood flow volume in donors after laser surgery [15, 16]. DVARF and UVPF, as abnormal venous Doppler, have been regarded to be signs of deterioration of fetal oxygenation in intrauterine growth restricted fetuses [17]. Donor twin could have an aspect as intrauterine growth restricted fetuses, but these parameters were not associated with the IUFD of donors in this study. Further, the incidence of these findings in the veins of donors was much less than that of UAAREDV. However, it was notable that all 3 donors with DVARF ended in fetal demise; this suggests that DVARF might be an indicator of IUFD.

With regard to recipient twins, this analysis showed that there was no association between the preoperative ultrasound parameters and IUFD following SLPCV. These results were consistent with those in a previous study [10]. UAAREDF, which was an important factor in donors, was noted in only one recipient and this fetus was born alive. Many of the recipient twins had abnormal venous velocities before SLPCV, where DVARF and UVPF were observed in 34.6 and 59.6% of the 52 fetuses, respectively. However, neither of these was correlated with IUFD. Of the 52 recipients, 12 (23.1%) showed hydropic symptoms prior to surgery. Three of the 4 recipients with IUFD had shown a few hydropic signs, while 9 hydropic recipients resulted in live-birth.

In comparison with other treatment options, laser surgery for TTTS has resulted in a much better perinatal outcome. In this situation, we anticipate a problem that needs to be overcome: how could the rate of IUFD be decreased after SLPCV? As mentioned above, UAAREDF in donors, as the preoperative prognostic factor for IUFD, may reflect both the placental insufficiency and fetal hypotension. If intraoperative transfusion between twins via placental vascular anastomoses could impact the blood volume of each twin, as suggested by Martinez et al. [10], laser coagulation of arteriovenous anastomoses from the donor to the recipient prior to arteriovenous anastomoses from the recipient to the donor should be adopted for cases with UAAREDF in donors. This may prevent not only the postoperative severe fetal anemia but also IUFD in donors. However, further evaluation of the pre and postoperative fetal hemodynamic status is required for understanding the impact of intraoperative blood transfusion between twins on their prognosis.

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RESEARCH LETTER

Prenatal rupture of right ventricular diverticulum: a case report and review of the literature

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KEY WORDS: ventricular diverticulum; fetoscopic laser photocoagulation; pericardial effusion

INTRODUCTION

Congenital cardiac diverticulum is a rare abnormality that may occur as an isolated malformation. Few cases diagnosed in fetal life have been reported. We report a case of right ventricular diverticulum below the tricuspid valve leading to intrauterine fetal death. This is the first report of cardiac diverticulum after fetoscopic laser photocoagulation of the chorioangiopagus for the treatment of twin–twin transfusion syndrome (TTTS).

CASE REPORT

A 25-year-old healthy nulliparous woman had a natural pregnancy of monochorionic diamniotic twins. She was referred owing to remarkable difference in amniotic fluid volume between the fetuses at 19 weeks of gestation. She was diagnosed on the third stage of Quintero's classification for TTTS, because stuck-twin phenomenon and absence of end-diastolic flow in the umbilical artery of the donor were found. There were no abnormal echocardiographic findings in the recipient fetus. She underwent selective fetoscopic laser photocoagulation of the 13 communicating vessels for the treatment of TTTS at 20 weeks of gestation. The donor fetus died one day after operation. In the recipient fetus, a high echogenic focus on the right ventricle and mild pericardial effusion were depicted at 21 weeks of gestation (Figure 1(a)). Further, ultrasound imaging at 24 weeks of gestation demonstrated an area of myocardial discontinuity just below the tricuspid valve, leading to a thin-walled saccular dilatation (7 mm × 10 mm) contained within the pericardial space (Figure 1(b)). Color-flow mapping and pulsed-wave Doppler imaging showed bidirectional flow into and from this structure, compatible with a cardiac ventricular diverticulum (Figure 1(c)). No other structural abnormalities were identified. There was no evidence of maternal or fetal infection. The woman was hospitalized at 25 weeks of gestation. Low-degree pericardial effusion in the fetus was still detected but no further increase was observed. The cardiac function followed a normal course. However, intrauterine fetal death occurred at 29 weeks of gestation. The cause of fetal death was unknown because postmortem examination was declined. However, expansion of the heart and remarkable increase in pericardial effusion were depicted on ultrasonography, suggesting a rupture of the ventricular diverticulum (Figure 1(d)).

A cardiac ventricular diverticulum is a localized protrusion of the wall of the cardiac ventricle with a narrow connection to the ventricle. In contrast, a cardiac aneurysm has a wide connection to the ventricle (Hamaoka *et al.*, 1987). The pathogenesis of ventricular diverticulum remains unknown. It is generally recognized that the wall of a diverticulum contains the three layers of a normal cardiac wall (peri-, myo-, and endocardium) whereas the myocardium of a true aneurysm is intermingled with fibrous tissue (Carles *et al.*, 1995). However, the two terms are often used interchangeably in the literature. In the present case, a diagnosis of diverticulum was made because jet flow was observed indicating a narrow connection to the ventricle.

DISCUSSION

The etiologies of cardiac diverticula and aneurysms in fetal life are poorly understood. They may occur as a result of focal weakening of the ventricular wall due to an interruption during embryogenesis, infection, or localized ischemia of the ventricular wall due to stenosis, hypoplasia or intimal proliferation of the coronary arteries (Carles *et al.*, 1995; Cavalle-Garrido *et al.*, 1997) McAuliffe *et al.* reported two cases in which the diverticula were detected in the first trimester, suggesting that these defects may occur early in pregnancy or even during embryogenesis (McAuliffe *et al.*, 2005).

It is interesting that this case was discovered after the demise of one twin following fetoscopic laser photocoagulation for the treatment of TTTS. Despite successful laser therapy, there is still a potential for neurological pathology in the twins, particularly if one subsequently demises, likely as a consequence of persistent

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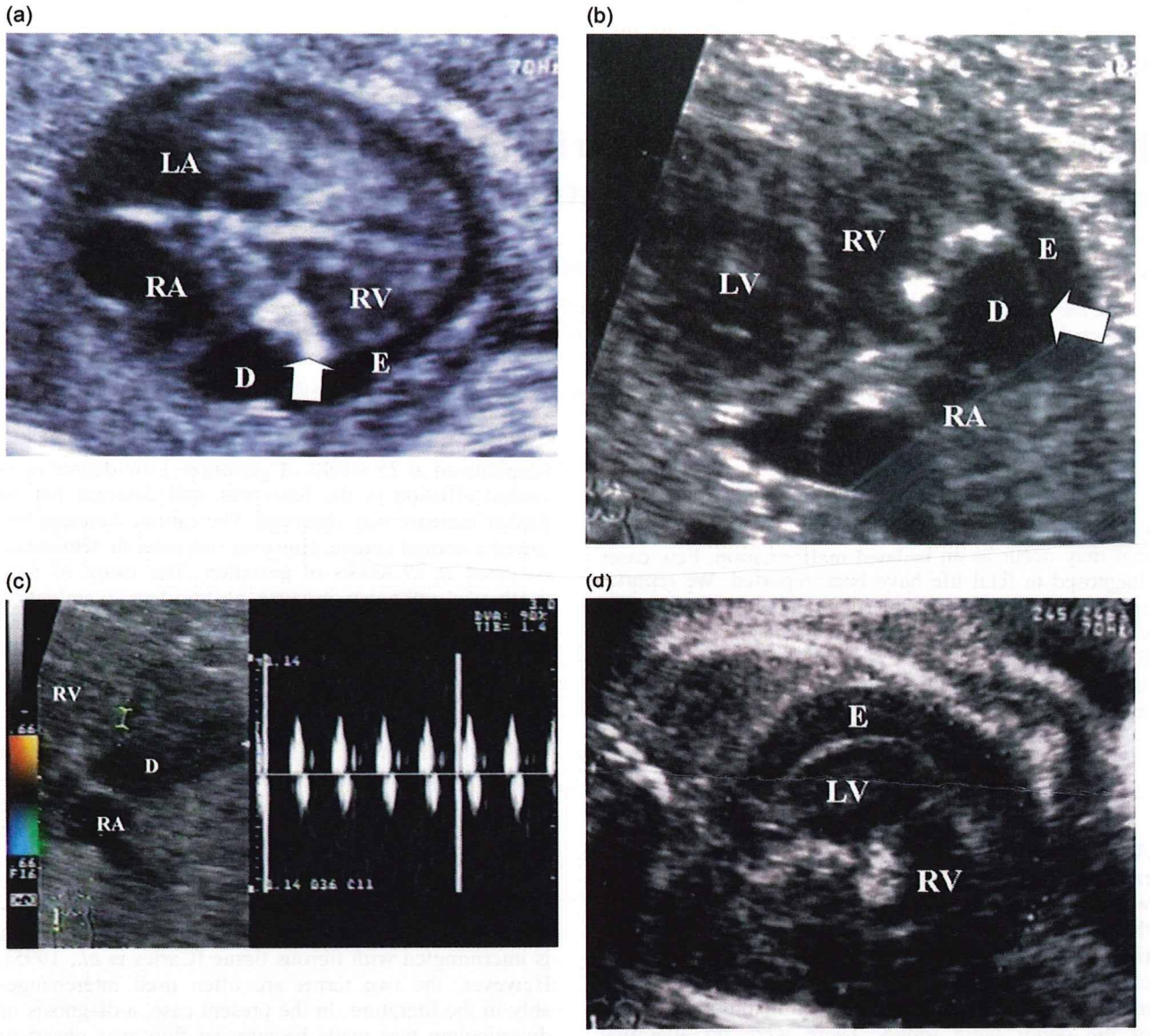

Figure 1—(a) Cardiac ultrasound imaging at 21 weeks of gestation. A high-echogenic focus (arrow) on the right ventricle (RV) and mild pericardial effusion (E) are depicted. LA: left atrium; LV: left ventricle, D: diverticulum, (b) Cardiac ultrasound imaging at 24 weeks of gestation. A thin-walled saccular dilatation (arrow) is identified just below the tricuspid valve. RV: right ventricle; LV: left ventricle; RA: right atrium; E: pericardial effusion; D: diverticulum, (c) Pulsed-wave Doppler imaging at 24 weeks of gestation. Bidirectional flow into and from the cardiac diverticulum is shown. RA: right atrium; RV: right ventricle; D: diverticulum; (d) Cardiac ultrasound imaging just after fetal death. Expansion of the heart and a remarkable increase in pericardial effusion (E) are depicted. RV: right ventricle; LV: left ventricle

vascular connections between the twins (Marton *et al.*, 2002). Marton *et al.* reported a case with left chamber myocardial infarction of the heart in the recipient twin in TTTS (Marton *et al.*, 2002). High-echogenic focus in the myocardium of the recipient twin has been described and is thought to perhaps reflect an area of infarction or at least ischemia. Tennstedt *et al.* reported that the echogenic, intramyocardial focus described at the prenatal sonographic examination appeared histologically as coarse, focal calcifications surrounded by fibrotic tissue (Tennstedt *et al.*, 2000). Abnormal development of the microvasculature, involving terminal branches of the coronary artery leading to early ischemic changes in the papillary muscle, has been suggested as the etiology in some cases (Tennstedt *et al.*, 2000). Therefore, it is suggested that this ventricular diverticulum may be a consequence of myocardial ischemia caused by TTTS or fetoscopic laser photocoagulation. Accumulation of the reported cases would answer the question why this might have happened in the present set of twins and not in others.

Our search of the literature identified 34 reported cases of congenital ventricular diverticulum or aneurysm diagnosed during the prenatal period (Carles *et al.*, 1995; Cavalle-Garrido *et al.*, 1997; Bernasconi *et al.*, 2004; McAuliffe *et al.*, 2005; Prefumo *et al.*, 2005; Gardiner *et al.*, 2005; Del Rio *et al.*, 2005). Table 1 summarizes 35 cases including the present case. The ventricular diverticulum or aneurysm was found at the right ventricle in 14 cases and at the left ventricle in 21 cases.

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Table 1—Summary of clinical variables in 35 cases (including the present case) of cardiac diverticulum or aneurysm reported in the literature

Case No.	Diag-nosis	GA at diagnosis	Location	Reason for referral	Outcome	Reference.
1	A	32	Apex/LV	Arrhythmia	Asymptomatic up to 2Y	Gembruch 1990
2	D	33	Apex/LV	CM	Alive	Kitchiner1990
3	A	33	Lateral wall/LV	ND	Surgical resection	Jacobson1991
4	D	31	Below TV	Abnormal 4CV	Asymptomatic up to 1Y	Hornberger1994
5	A	28	Apex/LV	Arrhythmia	Asymptomatic up to 4M	Hornberger1994
6	A	25	Apex/LV	Arrhythmia	Asymptomatic up to 10M	Hornberger1994
7	D	13	Apex/LV	PE, arrhythmia	TOP at 14W	Carles1995
8	A	19	Apex/LV	Hydrops	Hydrops, TOP at 19W	Sepulveda1996
9	A	24	Apex/LV	PE	Hydrops, IUFD at 31W	Sherman1996
10	D	19	Apex/RV	PE	Asymptomatic up to 16M	Johnson1996
11	D	17	Apex/LV	PE	TOP at 22W	Cesko1998
12	D	36	Below TV	CM	Asymptomatic up to 18M	Cavalle-Garrido1997
13	A	21	Apex/LV	Abnormal 4CV	Asymptomatic up to 24M	Cavalle–Garrido1997
14	A	18	Apex/LV	Abnormal 4CV	Mild LVH, alive	Cavalle–Garrido1997
15	D	19	Apex/RV	PE	Asymptomatic up to 12M	Cavalle–Garrido1997
16	A	19	Below MV	Abnormal 4CV	IUFD (MR, hydrops) at 31W	Cavalle–Garrido1997
17	D	20	Apex/RV	PE	Asymptomatic up to 22M	Cavalle–Garrido1997
18	D	20	Below MV	PE	IUFD at 26W	Cavalle–Garrido1997
19	A	26	Apex/LV	PE, CM (MR+)	IUFD at 33W	Matias1999
20	A	21	Apex/LV	CM (MR+)	Neonatal death	Matias1999
21	A	22	Lateral wall/LV	CM	TOP at 23W	Matias1999
22	A	25	Apex/LV	Abnormal 4CV	Asymptomatic up to 12M	Pipitone2002
23	A	21	Below TV	Abnormal 4CV	Asymptomatic up to 6M	Pipitone2002
24	D	32	Apex/LV	ND	Asymptomatic up to 6M	Brachlow2002
25	A	24	Apex/RV	PE	Well going at 30W	McCaffrey 2002
26	A	29	Apex/LV	PE	ND	Sharma2002
27	D	24	Below MV	PE	IUFD (rupture) at 24W	Bernasconi2004
28	D	13	Apex/RV	PE	Term delivery	McAuliffe2005
29	D	16	Apex/RV	PE	Term delivery	McAuliffe2005
30	D	14	Apex/RV	PE	Asymptomatic up to 22M	Prefumo2005
31	D	12	Apex/LV	PE	Asymptomatic up to 17M	Prefumo2005
32	D	14	Apex/RV	PE, CM	TOP	Gardiner2005
33	D	14	Apex/RV	PE, CM	Term delivery	Gardiner2005
34	D	13	Apex/RV	PE	Term delivery, surgical correction	Del Rio2005
35	D	24	Below TV	HEF, PE	IUFD (rupture) at 29W	This report

GA: gestational age; A: aneurysm; D: diverticulum; RV: right ventricle; LV: left ventricle; TV: tricuspid valve; MV: mitral valve; CM: cardiomegaly; ND: not documented; 4CV: 4 chamber view; PE: pericardial effusion; MR: mitral regurgitation; HEF: high-echogenic focus; TOP: termination of pregnancy; IUFD: intrauterine fetal death; Y: years after birth; M: months after birth; W: gestational age in weeks.

In another aspect, the ventricular diverticulum/aneurysm was located at the apex in 26 cases, below the atrioventricular valve in 7 cases, and on the lateral free wall in 2 cases. The outcomes of 30 cases were documented well in these reports. Among them, 5 cases ended in termination of pregnancy. Intrauterine fetal death or early neonatal death occurred in 7 of the remaining 25 cases. When examined by location of the diverticulum or aneurysm, 4 of 7 subvalvular cases and 3 of 18 apical cases resulted in fetal or neonatal death. Ventricular diverticula located below the atrioventricular valves had significantly poorer prognosis compared with those at the apex (^{2} test, $p < 0.05$). This poor prognosis could be explained by the observation that they were often accompanied with a thin fibrous wall and/or regurgitation of valves.

Most cases of ventricular diverticulum have been diagnosed prenatally by ultrasound examination for other cardiac complications such as pericardial effusion, arrhythmia, cardiomegaly, or abnormal 4 chamber view (Table 1). Since the concept of the disease is not well known, many asymptomatic cases of ventricular diverticulum are probably not diagnosed and hence not reported. Further case reports are necessary to predict prenatal and postnatal outcome, which will allow efficient parental counseling.

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