

SUCCESSFUL TREATMENT OF TWIN–TWIN TRANSFUSION SYNDROME BY OCCLUSION OF PLACENTAL VESSEL ANASTOMOSES USING ENBUCRILATE

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SUMMARY

Objective: Twin–twin transfusion syndrome is a serious obstetric complication unique to monochorionic twin gestations. Occlusion of vessel anastomoses is recommended to improve the perinatal outcome.

Case Report: A 36-year-old, gravida 1, woman had a monochorionic twin pregnancy which was found to be affected by twin–twin transfusion syndrome at 26 weeks' gestation. The condition was successfully treated by occlusion of placental vessel anastomoses using enbucrilate under color Doppler ultrasonographic guidance. At 35 weeks of gestation, two male infants were delivered by cesarean section. The birth weights of the babies were 2,470 and 1,750 g, and both were thriving.

Conclusion: Targeted therapeutic ablation of vessel anastomoses involved in twin–twin transfusion syndrome using color Doppler ultrasonographic guidance is minimally invasive and may effectively obliterate interfetal transfusion, contributing to the survival of both twins. [*Taiwan J Obstet Gynecol* 2008;47(3):330–333]

Key Words: Doppler ultrasonography, monochorionic twin, twin–twin transfusion syndrome

Introduction

Twin–twin transfusion syndrome (TTTS) is a serious obstetric complication unique to monochorionic twin gestations. The prognosis is poor if the condition is untreated, with an overall perinatal mortality of 80% [1]. TTTS occurs when a donor twin perfuses a recipient twin through vessel anastomoses. Therefore, occlusion of the anastomoses is recommended to improve the perinatal outcomes of both twins. Recently, fetoscopic laser photocoagulation of the underlying anastomoses has emerged as a treatment of choice [2]. However, this is a technically challenging procedure that is available in only a few medical centers with fetal medicine

resources. We report the successful treatment of a case of TTTS using minimally invasive, ultrasound-guided percutaneous ablation of the anastomotic circulation by injection of enbucrilate into the involved vessels, a procedure that contributed to the subsequent survival of both twins.

Case Report

A 36-year-old primigravid woman first presented at our institution at 10 weeks' gestation for a routine first-trimester ultrasound examination. Sonography revealed a monochorionic, diamniotic twin pregnancy, consistent with the last menstrual period. The 12th week scan was normal with nuchal translucencies of 1.2 mm and 1.8 mm. Amniocentesis was performed at 15 weeks of gestation to exclude chromosomal abnormalities, and it showed that both twins had normal karyotypes. Neither fetus showed any malformation. The mother was then monitored every 2 weeks to check the



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fetal growth as well as to detect early signs of TTTS, using Doppler studies. Fetal echocardiography was normal in both twins at 17 weeks. At 19 weeks, there was a 12% discordance in fetal growth. A donor twin appeared “stuck” with no bladder filling, with normal arterial and venous Doppler findings. The operator noted moderate polyhydramnios (deepest vertical pool, 6.2 cm), reverse flow in the ductus venosus during atrial contraction, and holosystolic tricuspid regurgitation in the recipient twin; the heart size was normal. At 22 weeks, however, discordance in the amniotic fluid volume was more marked (deepest vertical pool, 1.2 cm in donor twin and 8.9 cm in recipient twin) and the degree of growth discordance had worsened to 16%. At 25 weeks, the recipient twin showed progressive cardiomegaly with a cardiothoracic ratio of 42%, hypertrophy of the myocardium, and tricuspid insufficiency. The donor twin had persistent oligohydramnios and its size was appropriate for a fetus that was 3 weeks younger than the recipient twin. One week later, the woman was admitted because of a sudden increase in abdominal tension and constant left lower quadrant abdominal pain. The polyhydramnios had increased (deepest vertical pool, 11 cm) and the uterus was tender to touch. Serial drainage amniocenteses were performed. However, the situation deteriorated, with evidence of a persistent, highly pathologic flow in the ductus venosus (negative *a* wave during atrial contraction) and a small pericardial effusion in the recipient twin. The donor twin still had normal arterial and venous flow. The patient was counseled about TTTS and possible treatment options. The parents were informed of the poor prognosis for both twins if the condition was untreated, and intervention to occlude placental blood flow was considered.

After approval of the hospital ethics commission and written informed consent from the parents, the placental chorionic plate was examined systematically with power Doppler ultrasonography to determine all vessel anastomoses. A 20-gauge needle was then directed into the vessel anastomoses within the placenta under ultrasonographic guidance. The needle was flushed with 10 mL 5% dextrose solution, followed by 2 mL enbucrilate (Histoacryl; Braun, Melsungen, Germany), diluted with lipiodol (Lipiodol Ultra-Fluid; Guerbet, Aulnay-sous-Bois, France) at a ratio of 1:5 [3]. The whole procedure took 15 minutes (Figure). Color Doppler ultrasound performed the next day confirmed the complete blockage and cessation of blood flow within all identified placental vessel anastomoses. The size of the recipient twin’s bladder normalized over the following weeks. Post-intervention Doppler ultrasonography of the umbilical artery showed improvement in

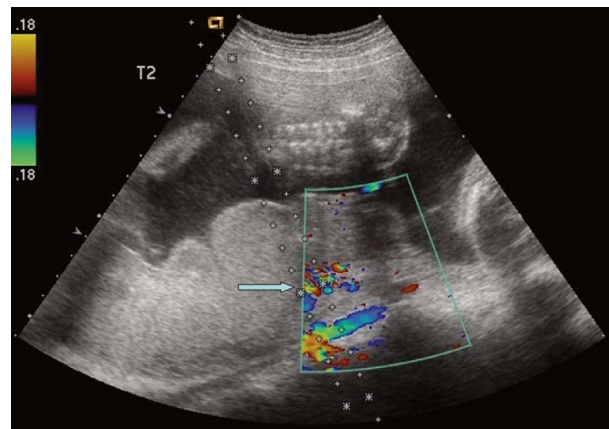


Figure. Ultrasonographic image shows the *in utero* appearance of the placenta of the monochorionic twin pair before embolization. The interfetal vascular anastomoses within the placenta are easily identifiable (arrow).

diastolic flow in the recipient twin. Amniotic fluid volume and bladder size in the donor twin returned to normal after 3 weeks. The growth rates of the two fetuses were normal, although the size discrepancy remained. Eight weeks after the procedure, at 35 weeks of gestation, the patient had prelabor rupture of membranes, and two boys were delivered by cesarean section. The Apgar scores for the recipient twin were 4 and 6 at 1 and 5 minutes, respectively, and those for the donor twin were 9 and 10 at 1 and 5 minutes, respectively. Birth weights of the recipient and donor twins were 2,470 and 1,750 g, respectively. Both babies were thriving at 6 months of age.

Discussion

Optimal management of TTTS is controversial. The clinical approach to pregnancies affected by TTTS is confounded by uncertainty regarding natural history, disease severity, gestation at presentation, and selection of patients for whom intervention may be indicated [4]. The prognosis is poor in cases diagnosed in the second trimester; untreated, perinatal mortality approaches 100% in these cases [1]. For this reason, several aggressive, even desperate treatment modalities have been attempted, including selective feticide, umbilical cord ligation and maternal digoxin therapy. These treatment methods have been only anecdotally successful and have created difficult ethical choices for parents and physicians. Serial drainage amniocenteses or amnioreduction is the most widely used therapy [4]. Although it reduces the complications of polyhydramnios, the basic pathology is not corrected. Uncontrolled series employing modern aggressive amnioreduction in which

amniotic fluid volume was reduced to normal have cited perinatal survival rates from 37% to 83%; the apparent risk of neurologic disabilities in survivors is 17–33%. The procedure-related risk of delivery is also considerable and is estimated to be 4% per procedure [5].

Recently, laser ablation of placental anastomoses under fetoscopic guidance in an attempt to improve survival has been reported. The most recently published series have shown a 55–82% perinatal survival rate and only a 4.2% neurologic handicap rate [2,5]. Fetoscopic laser ablation of placental vessels is a cause-oriented treatment for TTTS. However, its application is still limited to a few fetal medicine centers because of its invasiveness, and demands for high operator skill. Similar to other invasive intrauterine procedures, fetoscopy carries a risk of rupture of the amniotic membranes. This risk is estimated to be about 10% [2].

Because of their characteristic periodic, bidirectional interference pattern of blood flow, arterio-arterial anastomoses in monochorionic twins can be identified reliably *in utero* [6,7]. Recent developments in color and power Doppler ultrasonography have enabled obstetricians to assess the placental vessel anastomoses that produce the disequilibrium that causes TTTS [8]. Various alternative *in utero* interventions to ablate blood flow contributing to interfetal transfusion have been reported. In this case, we developed a technique of intrauterine therapy for TTTS by occlusion of placental vessel anastomoses with enbucrilate injection under color Doppler ultrasonographic guidance. Enbucrilate, also known as *N*-butyl-2-cyanoacrylate, is a liquid adhesive that polymerizes immediately upon contact with blood and other body fluids. Although controversial, it has been used as an embolic agent in medicine for almost three decades, notably in the treatment of bleeding esophagogastric and ectopic varices. Successful homeostasis has also been reported in bleeding peptic ulcers and Dieulafoy lesions; injection may also be used effectively for transcatheter arterial embolization. In obstetrics, it has been used successfully as an alternative to sutures for episiotomy closure [9] and for internal iliac artery embolization for treatment of massive obstetric hemorrhage [10]. Prenatal utilization of enbucrilate has been reported for the embolization of a large chorioangioma [3] and for vascular embolization in selective feticide in cases of TTTS [11].

To our knowledge, this is the first reported case in which ablation of interfetal blood flow associated with TTTS was accomplished with enbucrilate. When our patient presented with signs of TTTS at 26 weeks' gestation, the donor twin had intrauterine growth restriction and oligohydramnios, and the recipient twin had pathologic flow in the ductus venosus, pericardial

effusion, and polyhydramnios. These findings suggested that the donor twin had signs of hemodynamic decompensation and placental insufficiency due to loss of blood through transfusion to the recipient twin. Intervention to ablate blood flow to the recipient twin was recommended to improve the outcomes for both fetuses. This approach was selected, because the technique was relatively noninvasive and did not require any additional equipment. Furthermore, the procedure was neither time-consuming nor required a general anesthetic. Embolization has been described as a rare complication of enbucrilate injection. Sites of embolization after gastric varix injection include the lung, left renal vein, cerebral and coronary arteries, inferior vena cava, and portal and splenic veins [12]. However, a potential concern in the use of enbucrilate prenatally is the distance the agent can travel within the vasculature, with the possibility that it may reach the fetus resulting in fetal damage. Enbucrilate is probably the agent least associated with nontargeted organ embolization because of the small injected volume into the feeding artery and the rapid polymerization of the chemical within the placental area. Nonetheless, further study is required to establish the safety of this novel therapy for TTTS. Use of this technique is suggested for high-risk pregnancies in which both monochorionicity and placental vascular anatomy are reliably demonstrated. In this case, color Doppler ultrasonography was used to identify anastomoses that lay on the surface of the chorionic plate and those deep within the placenta.

In conclusion, targeted therapeutic ablation in TTTS with color Doppler ultrasonographic guidance is a minimally invasive technique. We presented our experience with successful intrauterine treatment with enbucrilate that effectively obliterated interfetal transfusion and contributed to the survival of both twins.

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