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Acardiac fetus complicating a triplet pregnancy: management and outcome

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Objective To report our experience with the management of triplet pregnancies complicated by an acardiac fetus.

Methods During the 5-year period from 2003 to 2008, five cases were identified. The prenatal sonographic findings, antepartum course, antenatal intervention if performed, and perinatal outcome of each case were reviewed.

Results Four pregnancies were spontaneously conceived and one was achieved by *in vitro* fertilization. Three pregnancies were dichorionic and two were monochorionic, and two acardiac fetuses were part of a monoamniotic set. All cases underwent an early sonographic examination, but the diagnosis was only made in the first trimester in only two cases, as the acardiac fetus was overlooked or inaccurately identified as a dead fetus in the remaining three cases. Early fetal demise before 12 weeks occurred in a case of monochorionic-triamniotic triplets. Percutaneous laser coagulation of the main intra-abdominal vessel was attempted at 17 weeks in two cases, with subsequent delivery after 34 weeks and perinatal survival of three of the four structurally normal fetuses. In the other two pregnancies which were managed expectantly, both were complicated by severe preterm delivery with perinatal survival of three of the four structurally normal fetuses. Overall, there were no survivors in one case, one twin survived in two cases, and two twins survived in the remaining two cases. None of the survivor had neurological sequelae.

Conclusions The presence of an acardiac fetus in a triplet pregnancy carries a high risk for poor pregnancy outcome, including fetal death and severe preterm labor. Prenatal intervention may be indicated in some cases, but does not prevent fetal death of the pump twin. Copyright © 2009 John Wiley & Sons, Ltd.

KEY WORDS: acardiac fetus; twin reversed arterial perfusion sequence; multiple pregnancy; prenatal diagnosis; fetal ultrasound; fetal therapy

INTRODUCTION

Acardiac anomaly, also know as twin reversed arterial perfusion (TRAP) sequence, is a unique complication of monochorionic twinning occurring with a reported incidence of 1/35 000 pregnancies (Benirschke and Kaufmann, 2000; Wong and Sepulveda, 2005). In this condition, a normal 'pump' twin supplies blood to its co-twin through a single artery-to-artery placental anastomosis, such that deoxygenated blood flows toward the co-twin via its umbilical artery in a paradoxical retrograde fashion. The abnormally perfused twin develops multiple lethal malformations secondary to incomplete and aberrant morphogenesis, the most common being acardia and acephaly (the 'acardius-acephalus' type; van Allen *et al*., 1983). In addition, the demand for circulatory support by the growing acardiac fetus places the pump twin at risk for high-output cardiac failure, polyhydramnios, and premature delivery, leading to perinatal death of the pump twin in 35% to 55% of cases (Moore *et al*., 1990; Healey, 1994).

The occurrence of an acardiac fetus in the context of a triplet pregnancy, while exceedingly rare (Benirschke and Kaufmann, 2000; Dahiya *et al*., 2004), is, as would be expected, associated with a poorer prognosis than a twin pregnancy, as the presence of an additional fetus increases the risk of perinatal morbidity and mortality. In this report, we describe five cases of a triplet pregnancy complicated by an acardiac fetus managed at our institutions in the last 5 years (2003–2008). In two of these cases, occlusion of the circulation to the acardiac fetus was attempted by percutaneous laser ablation of the intra-abdominal vessels.

CASE REPORTS

Case 1

A 35-year-old primigravida was referred to our unit at 10 weeks of gestation for sonographic evaluation of a dichorionic twin pregnancy in which an 'echogenic

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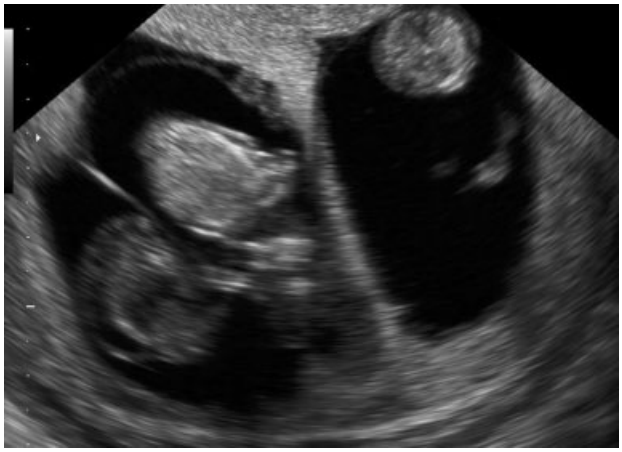
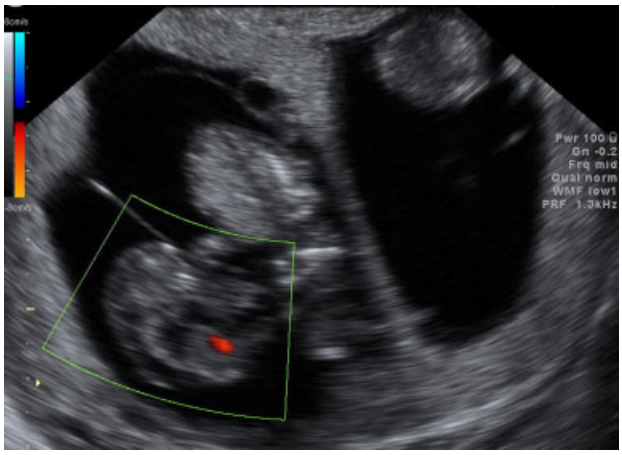
mass' in one of the sacs was first noted at 7 weeks of gestation. The mass measured 4 mm and increased to 10 mm at 8 weeks. Her history was significant for 3 years of infertility, and the current pregnancy was achieved by *in vitro* fertilization, with two fertilized embryos transferred at the eight-cell stage. Sonographic evaluation at referral revealed a dichorionic-triamniotic triplet pregnancy. The monochorionic set demonstrated a structurally normal twin measuring 41 mm in one amniotic sac and a 34-mm acardiac fetus in the other (Figure 1A and B). Of note, the pump fetus had an increased nuchal translucency thickness of 4.3 mm. Follow-up scans revealed growth of the acardiac fetus to 43 mm at 12 weeks and massive subcutaneous edema and increased size of the cystic components at 16 weeks. The parents were counseled regarding the expected prenatal course of continuous growth of the acardiac fetus and hemodynamic compromise of the pump fetus. Different management options including expectant management and intervention aimed to occlude the blood supply to the acardiac fetus were discussed at length (Tan and Sepulveda, 2003). Prenatal intervention was desired, and intrafetal ablation of the acardiac fetus' vasculature using ultrasound-guided interstitial laser was deemed the best option. After written informed consent, the procedure was performed as previously reported (Sepulveda *et al*., 2004a) without complication at 17 weeks. Subsequent prenatal course was uncomplicated except for suboptimal growth and progressive oligohydramnios of the pump fetus noted during the third trimester. At 34 weeks, the patient presented with preterm labor and breech presentation of the second fetus. A cesarean section was performed, delivering a normal female triplet weighing 2305 g and with Apgar scores of 9 and 10 at 1 and 5 min, respectively. The pump fetus weighed 1795 g and had Apgar scores of 9 and 9. The papyraceous acardiac fetus weighed 14 g and measured 10 cm (Figure 1C). The infants were discharged in good condition after an uncomplicated neonatal course.


(A)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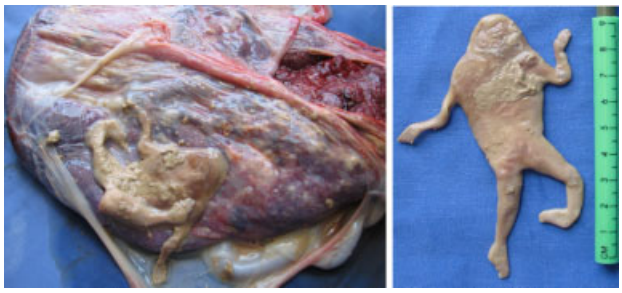
(C)

Figure 1—Case 1. (A) Transvaginal sonographic view of a dichorionic-triamniotic triplet pregnancy at 10 weeks. An acardiac fetus is seen in the lower left portion of the screen. (B) Color Doppler sonography shows reversed blood flow in the acardiac twin. (C) The placenta and acardiac fetus at the time of the delivery at 34 weeks. Interstitial laser ablation was performed at 17 weeks

Case 2

A 27-year-old primigravida was referred at 16 weeks of gestation for further evaluation of a dichorionic-triamniotic triplet pregnancy complicated by an acardiac fetus. An office scan at 11 weeks initially detected a dichorionic triplet pregnancy, in which one of the triplets was presumably dead. The diagnosis of TRAP sequence was made upon referral, at which time the acardiac fetus was larger than the pump fetus, which also had suboptimal interval growth and a velamentous insertion of the umbilical cord in the intertwin membrane (Figure 2). Using the same protocol as in case 1, ultrasound-guided intrafetal interstitial laser ablation was performed without complication at 17 weeks. The following day, Doppler sonography showed no blood flow in the acardiac fetus. However, a follow-up scan 6 days later showed intrauterine demise of the pump fetus, which was also noted to be hydropic. Subsequent prenatal course was uncomplicated for the surviving triplet. At 37 weeks, a cesarean section was performed due to early labor and breech presentation, delivering a healthy female infant weighing 2730 g and with Apgar scores of 9 and 9. After an uncomplicated neonatal course, she was discharged in good condition.

Case 3

A 33-year-old woman, gravida 3, para 1, was referred at 17 weeks of gestation for sonographic assessment

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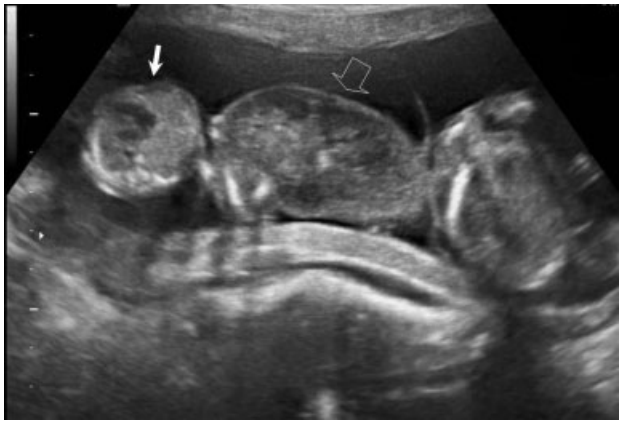

Figure 2—Case 2. Dichorionic-triamniotic triplet pregnancy at 17 weeks. Note that the acardiac fetus (open arrow) was larger than the pump twin (solid arrow)

of a monochorionic-diamniotic triplet pregnancy with one presumed dead fetus. A first-trimester sonographic examination at 12 weeks had shown a triplet pregnancy with two structurally normal fetuses measuring 54 and 55 mm, respectively, and a third fetus measuring 25 mm without cardiac activity. A second-trimester scan at referral led to the diagnosis of TRAP sequence with umbilical cord entanglement between the pump and the acardiac fetuses (Figure 3A). Serial sonographic examinations showed no development of polyhydramnios or signs of cardiac insufficiency in the pump twin. There was continuous growth of the acardiac fetus (Figure 3B), but no blood flow within its body was identified from 23 weeks onward, leading to a decrease in size of the acardiac mass (Figure 3C). Subsequent scans showed normal growth of the other fetuses. At 31 weeks, Doppler studies of the umbilical artery of the

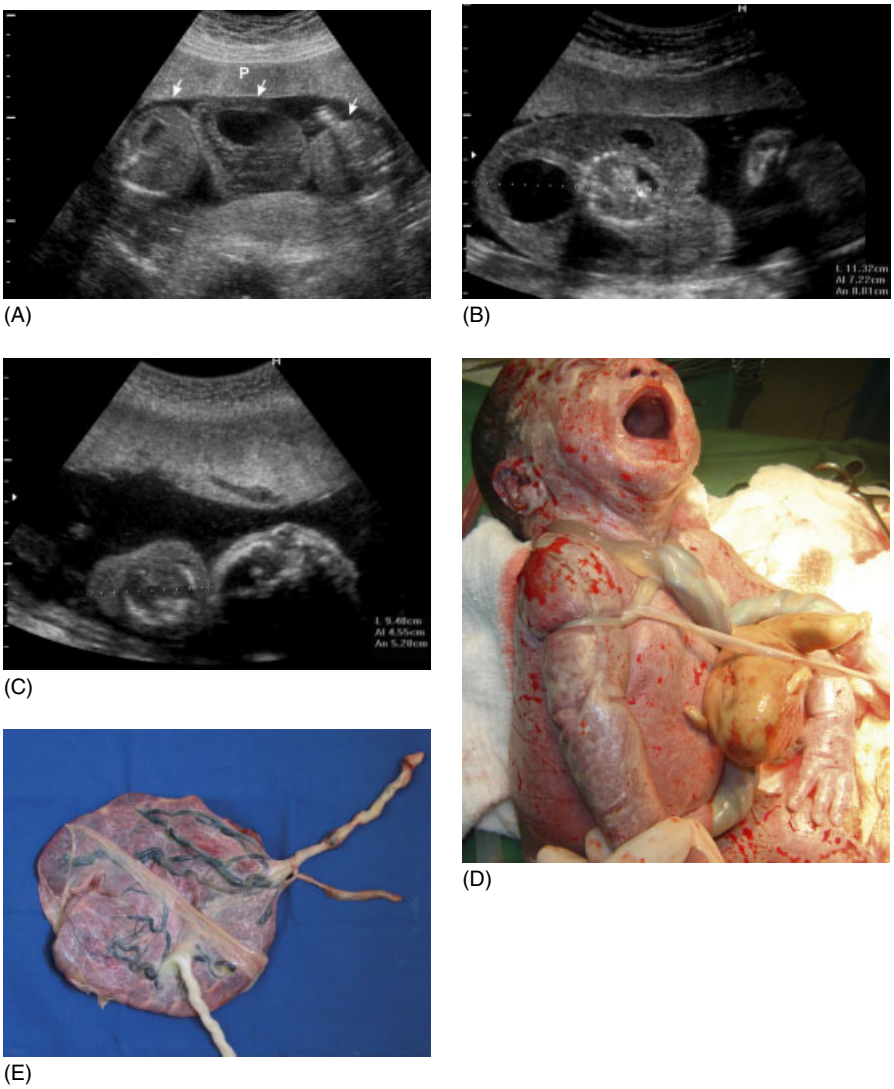

Figure 3—Case 3. (A) Monochorionic-diamniotic triplet pregnancy at 17 weeks. Arrows denote the transverse section view of the three fetuses. Note the size of the hydropic, acardiac fetus, and absence of polyhydramnios. P, single anterior placenta. (B) Increasing size of the acardiac fetus at the follow-up scan. (C) At 23 weeks, there was spontaneous cessation of blood flow to, and shrinkage of, the acardiac fetus. (D) The monoamniotic fetuses at the time of the delivery at 31 weeks. There was tight entanglement of the acardiac twin's umbilical cord around the pump twin's arm and umbilical cord. Note the acardiac fetus in front of the pump twin's abdominal wall. (E) The monochorionic-diamniotic placenta

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pump twin showed fetal compromise and a cesarean section was performed, delivering two structurally normal fetuses weighing 1320 g and 1640 g, both with Apgar scores of 8 and 9 at 1 and 5 min, respectively. Within the monoamniotic set was an 80 g acardiac, acephalic fetus, with tight entanglement of its umbilical cord around the umbilical cord and right arm of the pump twin (Figure 3D and E). Both surviving infants required minimal neonatal support and were discharged in good condition.

Case 4

A 39-year-old woman, gravida 2, para 1, underwent a first-trimester sonographic examination at 11 weeks, at which time a dichorionic twin pregnancy was diagnosed. Subsequent scans at 16 and 20 weeks, however, revealed a dichorionic-diamniotic triplet pregnancy with a presumably dead fetus complicating the monoamniotic pair. The significant growth of the 'dead' fetus and observation of incidental fetal movements during real-time sonographic examination led to the diagnosis of TRAP sequence at 23 weeks. At referral, the pump twin was growth restricted (estimated fetal weight of 423 g), had increased amniotic fluid volume, and entanglement of the umbilical cords was sonographically visualized. The other fetus was growing appropriately (estimated fetal weight of 725 g) and had normal anatomy and amniotic fluid volume. Sonographic evaluation 2 weeks later showed intrauterine demise of the pump fetus and polyhydramnios in the monoamniotic sac. An uneventful amniodrainage was performed to decrease intrauterine pressure and uterine contractions. Subsequent prenatal course was complicated by gestational diabetes, and corticosteroids were used to enhance lung maturity in anticipation of preterm delivery. At 32 weeks, a healthy male fetus weighing 1660 g was delivered by cesarean section because of early labor. The infant did well with minimal neonatal support and was discharged home on day 22.

Case 5

A 38-year-old woman, gravida 4, para 3, presented for a first-trimester scan at 7 weeks of gestation, at which time a monochorionic twin pregnancy with two live fetuses measuring 13 and 12 mm was diagnosed. Follow-up transvaginal scan at 10 weeks, however, revealed a triplet monochorionic-triamniotic pregnancy with two viable fetuses and an additional fetus without cardiac activity. Further color Doppler sonography showed intrafetal blood flow, confirming the presence of an acardiac fetus. The patient was scheduled for a nuchal translucency scan at 12 weeks, at which time intrauterine demise of the two normal fetuses was diagnosed. Dilatation and curettage was performed, and therefore no pathological examination was able to be performed.

DISCUSSION

The rarity of acardiac anomaly complicating a triplet pregnancy is evident from the few reports published in the literature. In 1985, before the widespread use of prenatal sonography, van Groeninghen *et al.* (1985) reviewed 360 published cases of acardiac fetus; only 3% ($n = 12$) occurred in a triplet pregnancy. Similarly, in a review of 184 pregnancies complicated by an acardiac fetus published from 1960 to 1991, Healey (1994) found a slightly higher prevalence of triplets of 8% ($n = 14$). More recently, Dahiya *et al.* (2004) found fewer than 20 cases published. Regarding pregnancy outcome, a recent review involving 13 triplet pregnancies complicated by an acardiac fetus showed that ten (77%) miscarried or delivered before 32 weeks with an invariable poor pregnancy outcome for the pump fetus (Nader *et al.*, 2009). Only two of these cases were diagnosed in the first trimester (Holmes *et al.*, 2000; de Catte *et al.*, 2002), and invasive treatment to interrupt the blood flow to the acardiac fetus was attempted in two cases (Schild *et al.*, 1998; Holmes *et al.*, 2000). Our group also reported a monochorionic-diamniotic triplet pregnancy in which percutaneous intrafetal monopolar coagulation was performed at 16 weeks, with intrauterine demise of the normal fetuses within the week after the procedure (Sepulveda *et al.*, 2003).

This report describes five additional cases of triplet pregnancies complicated by an acardiac fetus, the largest series reported thus far. Table 1 displays the main clinical and sonographic findings in our cases. The definitive diagnosis was made in the first trimester in two cases, in one of which the pregnancy was achieved with assisted reproductive techniques prompting serial first-trimester scanning. The remaining three cases could also have been diagnosed in the first trimester if resources permitted early sonographic evaluation by an experienced operator. Early diagnosis in these cases is important, as it allows an accurate determination of chorionicity. As TRAP sequence only occurs in monochorionic pregnancies, accurate determination of chorionicity is crucial to assess the prognosis of the pregnancy. If the third fetus has its own placenta, and hence the pregnancy is dichorionic, this particular fetus is protected against hemodynamic imbalance if death of the pump twin occurs, either spontaneously or as a complication of an invasive treatment. However, if the entire pregnancy is monochorionic, the fragile and complex vascular network among the three fetuses means that any hypotensive event, including the attempt to arrest the circulation to the acardiac fetus, could result in hemodynamic complications to all fetuses. Amnionicity is also important, as monoamniotic pregnancies carry the additional risk of tight cord entanglement, as seen in two of our cases. First-trimester diagnosis also prompts closer surveillance of the pregnancy, with earlier opportunity for surgical intervention to ablate the vascular supply to the acardiac fetus in order to decrease the hemodynamic consequences and the mass effect on the fate of the pregnancy.

There has been extensive controversy regarding the best invasive treatment of pregnancies complicated with

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Table 1—Acardiac fetus complicating a triplet pregnancy. Case descriptions

Case	MA (years)	Para	GA (weeks) at diagnosis	Chorionicity	Prenatal intervention	Pregnancy outcome
1[a]	35	0	10	Dichorionic-triamniotic	Percutaneous intra-abdominal interstitial laser ablation at 17 weeks	Cesarean section of both viable fetuses at 34 weeks. 2305 g, A&W. [b]1795 g, A&W
2	27	0	16	Dichorionic-triamniotic	Percutaneous intra-abdominal interstitial laser ablation at 17 weeks	IUD of pump twin at 18 weeks. Cesarean section of one viable fetus at 37 weeks. 2730 g, A&W
3	33	1	17	Monochorionic-diamniotic	None	Spontaneous cessation of blood flow to the acardiac fetus at 23 weeks. Cesarean section of both viable fetuses at 31 weeks. 1320 g A&W. [b]1640 g A&W
4	39	1	23	Dichorionic-diamniotic	Amniodrainage	IUD of pump twin at 26 weeks. Cesarean section of one viable fetus at 32 weeks. 1660 g, A&W
5	38	3	10	Monochorionic-triamniotic	None	IUD of both viable fetuses at 12 weeks

MA, maternal age; GA, gestational age; A&W, alive and well; IUD, intrauterine death.
[a] Pregnancy achieved by *in vitro* fertilization.
[b] Pump fetus.

an acardiac fetus (Sepulveda and Sebire, 2004b). Currently available invasive options include occlusion of the umbilical cord or intrafetal vessels with injection of chemosclerosants, monopolar and bipolar coagulations, percutaneous interstitial laser, and fetoscopic ligation or coagulation of the cord or placental anastomoses (Tan and Sepulveda, 2003; Sebire *et al*., 2006). Interstitial laser ablation of the intra-abdominal vessels has been described as one of the less-invasive techniques, which can be safely carried out in early second-trimester acardiac twins (Jolly *et al*., 2001; Soothill *et al*., 2002). It consists in the use of an 18-gauge needle guided by color Doppler sonography through which the laser fiber is passed. Once in close proximity to the main abdominal or pelvic vessel of the acardiac twin, laser energy is applied with resulting occlusion of the neighboring vessel. As this procedure involves the use of a thin needle, it can safely be performed in early pregnancy and should not be more cumbersome than a chorionic villous sampling, which uses a similar technique. Because of these advantages, this method was considered the best option and was carried out without complication at 17 weeks in two of our cases, one of which resulted in the delivery of normal twins at 34 weeks. In the second case, however, the pump fetus died 6 days after the procedure.

The pathophysiologic mechanisms leading to the intrauterine demise of the pump twin after a seemingly successful procedure are not clear, but bleeding into the acardiac fetus and entrapment of blood may lead to severe anemia and death in the pump fetus in twin pregnancies (Sepulveda *et al*., 2008). This could be the result of incomplete occlusion or recanalization of the acardiac twin's main feeding vessel. Unfortunately, postmortem examination was not possible in our case in which laser ablation was used, as delivery occurred several months after the demise of the pump twin. To the best of our knowledge, based on a Medline search using the terms 'acardiac twin', 'acardius', 'TRAP sequence', 'twin reversed arterial perfusion sequence', and 'triplet pregnancy', these are the first cases in which percutaneous interstitial laser is used in the management of a triplet pregnancy complicated by an acardiac fetus. In triplet pregnancies, previous reports have described the use of radiofrequency (Lee *et al*., 2007), monopolar coagulation (Holmes *et al*., 2000; Sepulveda *et al*., 2003), and embolization (Schild *et al*., 1998) with variable success rates. Our experience with the cases presented here supports the feasibility of early laser ablation as another treatment option in triplet pregnancies complicated by an acardiac fetus. However, further experience with increasing number of cases is needed to evaluate the safety of this procedure to the surviving fetuses.

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