Twin Reversed – Arterial Perfusion Sequence: The Experience of a Tertiary Referral Hospital in the Philippines with Acardiac Twinning

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ABSTRACT

Twin reversed-arterial perfusion sequence is a rare complication of monochorionic pregnancies. It is characterized by the hemodynamic dependence of the recipient twin on a pump twin. The recipient twin exhibits lethal malformations. The pump twin's survival is threatened by congestive heart failure and prematurity. Mortality rate ranges from 50% to 75% if untreated. Mortality is reduced to 13.6% with surgical intervention.[1] Five cases of twin reversed-arterial perfusion sequence were seen in the Philippine General Hospital, a university hospital and tertiary referral center. All cases had acardiac twins and were managed conservatively. The first three cases were previously reported. Two additional cases were encountered in 2007-2008 and are here presented. The first case was in a 41 year old G8P7 (7007) with diffuse toxic goiter and hypertension. The pregnancy was plagued with polyhydramnios and cardiac decompensation of the pump twin resulting in fetal death- in-utero. The second case was in a 37 year old G3P2 (2002) who had no medical co-morbidities. There were no risk factors and the outcome was a term livebirth.

Key Words: acardiac twins, pump twin, Twin Reverse Arterial Perfusion Sequence (TRAP) sequence, Chorangiopagus parasiticus (CAPP)

Introduction

The twin reversed-arterial perfusion (TRAP) sequence is a rare complication of monochorionic twinning or high order gestation. The incidence of TRAP sequence is one in 35,000 pregnancies, 1% of monochorionic twin pairs or one in 30 monochorionic triplets.[2,3,4] TRAP sequence is characterized by the hemodynamic dependence of a recipient twin on a donor twin commonly called the pump twin. Blood flows from the umbilical arteries of the pump twin through arterio-arterial and/or veno-venous anastomoses at the chorionic plate and into the recipient twin in a retrograde manner (entering by the umbilical artery and leaving by the umbilical vein). The recipient twin receives deoxygenated blood from the pump twin. During perfusion of the recipient twin, further deoxygenation of the blood occurs. The blood bypasses the placenta as it flows through the veno-venous anastomosis and is returned to the venous circulation of the pump twin and thus, contributes to chronic hypoxemia and growth restriction. The pump twin typically has normal morphology and karyotype. The recipient twin, on the other hand, exhibits a wide spectrum of developmental and reductional malformations like acardia or acephaly, and a relative excess of edematous tissue.[3] Most acardiac fetuses are found in twin pregnancies and only 8% in triplets.[5] Complications of TRAP sequence include: polyhydramnios which may result in premature rupture of the amniotic membranes, premature labor and delivery, congestive heart failure of the pump twin (high output failure), and intrauterine death of the pump twin. Risk factors for pump twin mortality are: high acardiac twin-to-pump twin weight ratio, especially if greater than 70%; acardiacus ancephs; low umbilical artery pulsatility index; and a rapid growth rate of the acardiac twin.[6] The mortality rate of the pump twin is 50% to 75% with expectant management compared with 13.6 % mortality rate if fetal surgery is performed (p<.001).[1,3] A myriad of interventions has been applied to treat TRAP sequence and most focus on the occlusion of the circulation to the acardiac twin. Presented are cases of TRAP sequence with acardiac twinning admitted to the Philippine General Hospital and managed conservatively.

To the author's knowledge, five cases of acardiac twinning were admitted to the Philippine General Hospital. Acosta-Sison, Aragon and De la Paz, in an article published in 1946 reporting the first case of monoamnionic twin pregnancy in the Philippine General hospital (first report in the Philippines), mentioned encountering an acardiac twin the size and shape of a goose egg in a monochorionic, monoamnionic twin pregnancy.[7] The second case was documented in 1996 by Llamas-Clark who initially thought that the acardiac twin was a sacrococcygeal teratoma on ultrasound.[8] The third case was reported by Ramos–Costa in 2004. It was in a 27 year old, segundigravid who was admitted to the Philippine General Hospital in 2001. Late in the second trimester of her pregnancy, she experienced low back pain radiating to the right flank and hypogastrium with associated fever, vomiting and dysuria. An abdominal ultrasound requested by her private physician was interpreted as a twin gestation with demise of one twin. She was referred to a tertiary hospital (Philippine General Hospital) for further management and was subsequently admitted. Admitting diagnosis was: pregnancy uterine 22 weeks and five days by amenorrhea, 20 weeks by early ultrasound aging, twin gestation with intrauterine demise of one twin and acute pyelonephritis. Parenteral antibiotics

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were administered and the symptoms of pyelonephritis resolved after two days. Based on findings on repeat ultrasound, the diagnosis was revised to acardiac twinning. The pregnancy was monitored for a month with serial biometry and biophysical profiles. Since the maternal and pump twin's condition remained stable, she was discharged and monitored on an outpatient basis. At 34 weeks and three days gestation by amenorrhea (31 weeks and five days by sonographic aging), the pump twin showed signs of hydrops, mild cardiomegaly and hepatomegaly on ultrasound. The woman was then re-admitted for closer monitoring of the pregnancy. On admission, the woman was ambulant, not in cardiorespiratory distress, afebrile with stable vital signs. Pertinent findings were: globular abdomen, fundic height of 35 cm, twins in breech-cephalic presentation, combined estimated fetal weight of 2.2 kilograms, fetal heart tones of 150 per minute heard at the left lower quadrant, and a closed, uneffaced cervix. She was not in labor. Dexamethasone 12 mg every 12 hours for four doses was given to induce lung maturation. Close fetal surveillance was done. Daily non-stress testings were reactive and biophysical profile scores remained 10/10. Fetal 2-D echocardiography showed cardiomegaly with mild right atrial and left ventricular enlargement, and severe tricuspid regurgitation. There was neither pericardial effusion nor evidence of hydrops fetalis. A consensus was reached by the obstetric service handling the patient and the pump twin was delivered by primary low segment cesarean section at 35 weeks and two days by amenorrhea (32 weeks and four days gestation by early ultrasound aging). Justification for the decision was that a course of steroids for pulmonary maturity was completed, the estimated fetal weight of the pump twin was 1,500 grams (a 70% chance of survival was associated with this weight) and cardiac dysfunction had set in as signified by cardiomegaly with severe tricuspid regurgitation. Pregnancy outcomes were: Twin A was the acardiac twin, male, weighing 500 grams with the head, trunk and upper extremities absent. Autopsy later revealed absence of cardiac tissue confirming the diagnosis. Twin B, the pump twin, was a live born male, weighing 1,600 grams, appropriate for age, APGAR score of 8 becoming 9, 32 weeks by pediatric aging and morphologically normal. The pump twin, however, succumbed to nosocomial sepsis after 17 days stay at the nursery. The mother's postoperative course was unremarkable. She was discharged well on the third postoperative day. The discharge diagnosis was: pregnancy uterine, twin gestation breech-cephalic, preterm; Twin A: Acardiac twin, Twin B: livebirth with fetal hydrops; and neonatal death secondary to sepsis.[8]

Presented are two additional cases of acardiac twinning encountered in the year 2008.

Case 1:

A case of acardiac twinning in a 41 year old, G8P7 (7007) with Diffuse Toxic Goiter diagnosed in 2006 and very poor medication compliance (Tapazole). Twinning was diagnosed by sonography performed at 23 weeks and one day gestation for uterine size larger than gestational age. The sonographic examination was performed in a hospital in the province and findings were interpreted as diamnionic, dichorionic twinning with intrauterine fetal death of a hydropic twin; and Polyhydramnios in both amniotic sacs. Twin to twin transfusion syndrome was entertained.

At 25 weeks and six days of gestation, the woman was admitted to the Philippine General Hospital. She was referred by a hospital in the province for difficulty of breathing and palpitations of one week duration. The diagnosis on admission was pregnancy uterine 25 weeks and six days by amenorrhea, twin gestation, cephalic–breech in preterm labor; to consider fetal death in-utero and fetal hydrops of twin B; Grandmultiparity; Diffuse Toxic Goiter in impending storm; Chronic hypertension with superimposed preeclampsia; Anemia, multifactorial. She presented in the emergency room ambulant but in cardiorespiratory distress. Her vital signs were as follows: Blood pressure: 150/90; heart rate: 120 beats per minute; respiratory rate: 26 per minute; and temperature: 37.8°C. The abdomen was globular with prominent veins. Fundic height was 36 cm, large for gestation. The estimated combined fetal weight was 3.8 to 4.0 kilograms. Fetal movements were discerned and muffled fetal heart tones of 150 beats per minute were auscultated at the right lower quadrant. Only a single set of fetal heart tones was appreciated. Mild uterine contractions with an interval of five minutes and duration of 15 seconds were documented. On internal examination, the cervix was soft, smooth, dilated to 3 to 4 cm and 30% effaced. Amniotic membranes were intact. The presenting twin was in cephalic presentation with the head at station -2. Fine finger tremors were appreciated. The patient had a Burch and Wartofsky's scoring of 35 (heart rate 120 = 15, temperature 37.8 °C = 10, precipitant history = 10). Urine dipstick was +2 albumin. Twenty four-hour total urine protein however, was only 124g. The woman's condition was stabilized with propylthiouracil and propranolol for the thyroid condition; antihypertensives and magnesium sulfate seizure prophylaxis for hypertension.

The congenital anomaly scan and Doppler velocimetry study revealed an intrauterine twin pregnancy with a single, high lying, anteriorly implanted, immature (grade II), monochorionic, diamnionic placenta (an intervening membrane was visualized). Twin A had good cardiac and somatic activities, and was in cephalic presentation. The biparietal diameter and femoral length were compatible with 27 weeks and two days and 25 weeks and two days, respectively. Abdominal circumference was 21.3 cm. Estimated fetal weight was 827 to 935 grams appropriate for gestational age. Twin A had fetal cardiomegaly with mild pericardial effusion, and polyhydramnios with the largest vertical pocket of 10.8 cm. Doppler flow studies showed end diastolic notching of the uterine arteries, otherwise normal indices for both the umbilical and uterine arteries. Twin B was an acardiac twin exhibiting somatic activity. The twin measured approximately 20 cm by 13 cm and weighed 446

grams. The largest vertical pocket of amniotic fluid was 4.5 cm, normohydramnios. Blood flow in the umbilical vessels unfortunately was not examined.

The preterm labor was managed expectantly due to the concomitant medical problems. Steroids in the form of intramuscular Dexamethasone 6 mg were administered every 12 hours for four doses to hasten pulmonary maturity. The impending thyroid crisis resolved and the hypertension controlled. The preterm labor spontaneously ceased. Cervical dilatation decreased to 1 to 2 cm from 3 to 4 cm but effacement remained at 30%, midpositioned. The pregnancy was allowed to continue with close fetal surveillance commencing at 28 weeks gestation. The long term plan was delivery at 34 weeks via cesarean hysterectomy pending medical clearance.

Maternal anemia was managed with transfusion of two units of packed red blood cells and oral hematinics. Low dose aspirin 80 mg per orem once a day was started to address the abnormal Doppler velocimetry findings. Propylthiouracil was discontinued when the FT4 and TSH levels were normal. Digoxin 0.25 mg once a day as inotropic support for the pump twin was started upon the advice of the pediatric cardiology service. The maternal condition remained relatively stable. The pump twin showed an interval weight gain of 148 to 150 grams per week or 324 to 329 grams per two weeks. There was no apparent deterioration in fetal cardiac function nor progression of polyhydramnios. The amniotic fluid largest vertical pocket fluctuated between 10.8 to 11.3 centimeters. Biophysical score remained 10/10. No adverse change in Doppler flow indices of the uterine and umbilical vessels was noted. The middle cerebral artery and ductus venosus however, were not measured.

After numerous consultations, consideration of the conditions in the nursery at the time, and at the urging of the pediatric cardiologist co-managing the case, the plan of management was changed. It was deemed best to terminate the pregnancy as close to term as possible to avoid complications associated with prematurity. The later could aggravate the fetal cardiac problem.

At 32 weeks and three days age of gestation (49th hospital day), there was a perceived decrease in fetal movements and irregular uterine contractions. Intrauterine demise of the pump twin was confirmed by sonography.

Both fetuses were delivered vaginally. The pump twin, twin A, was delivered spontaneously while the acardiac twin by partial breech extraction under general anesthesia. The discharge diagnosis was: pregnancy uterine, twin gestation, cephalic–breech; Twin A delivered preterm 32 weeks and six days via spontaneous vaginal delivery, male, birthweight 1,300 grams, appropriate for gestational age, stillbirth. Twin B delivered by partial breech extraction, chorangiopagus parasiticus (acardius acephalus); Diffuse toxic goiter clinically and biochemically euthyroid; Chronic hypertension; Anemia, multifactorial, corrected; Grandmultiparity. Autopsy findings were consistent with twin reverse-arterial perfusion sequence. Twin A was a male, 32 weeks by morphometry, 1,300 grams appropriate for age, pale (Figure 1 A & B). He was morphologically normal except for cardiomegaly with left ventricular

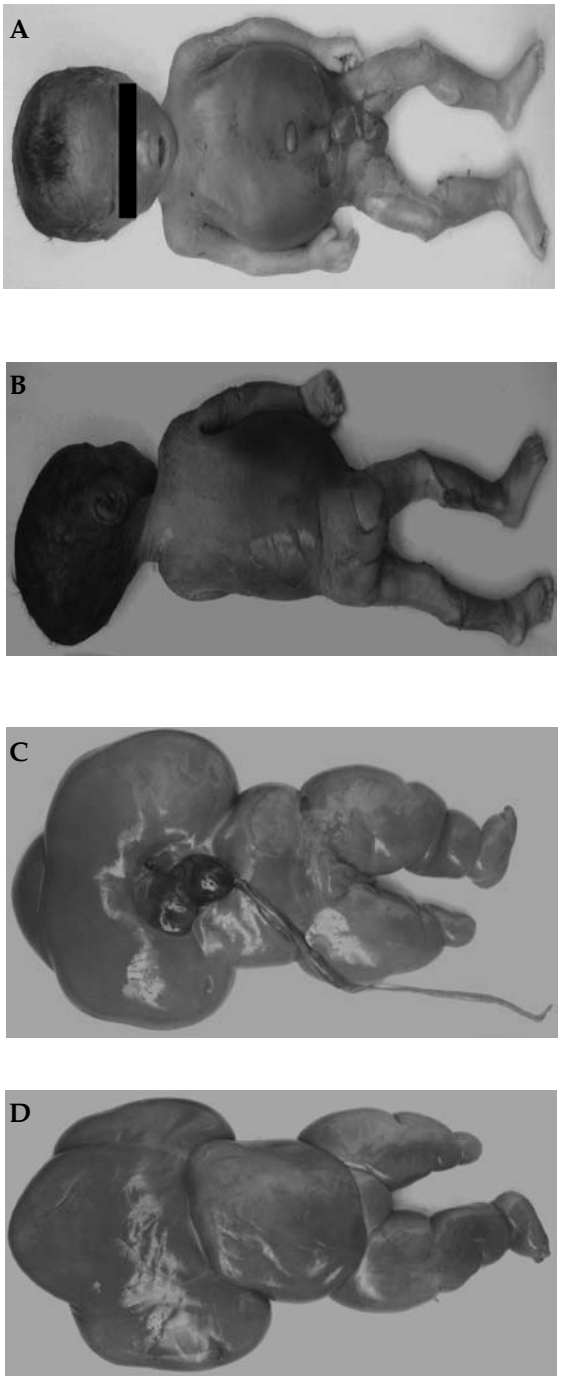

Figure 1. A&B, Twin A male, 32 weeks by morphometry, 1,300 grams, pale, macerated, morphologically normal except for cardiomegaly with left ventricular hypertrophy. C&D, Twin B acardius acephalus, male, 1,800 grams, 32 weeks by morphometry, edematous, absent esophagus, liver, pancreas and gallbladder; Meckel's diverticulum; imperforate anus with persistent cloaca; Omphalocele; Undescended testis; Fused kidneys; Oligodactyly, left foot; Pedal hypoplasia, right foot.

hypertrophy. The umbilical cord had three vessels. Twin B was a chorangiopagus parasiticus twin, (acardius acephalus), male, 1,800grams, 32 weeks by morphometry, edematous, with gastrointestinal malformations (Meckel's diverticulum, imperforate anus with persistent cloaca and absent esophagus, liver, pancreas and gallbladder); Omphalocele; Undescended testis; Fused kidneys (20 grams) "horseshoe" and lower extremity malformations (Oligodactyly, left foot; Pedal hypoplasia, right foot) (Figure 1 C & D). The umbilical cord had two vessels. The placenta was monochorionic, monoamnionic weighing 600 grams. Several superficial arterio-arterial and veno-venous anastomoses were documented (Figure 2).

Case 2:

This is a case of acardiac twinning in a 37 year old G3P2 (2002) that was initially mistaken to be a singleton pregnancy with a fetal sacrococcygeal teratoma. The woman was referred to the tertiary hospital for management of the latter. A congenital anomaly scan was done at 32 weeks age of gestation. There was no sonographic evidence of a sacrococcygeal teratoma. Instead, a 12.2 x 12.2 cm acardiac twin was noted coexisting with a morphologically normal co-twin (pump twin). There was a single monochorionic-diamnionic placenta, which was implanted anteriorly and high. Amniotic fluid volume was normal with an amniotic fluid index of 13.4 cm. Initial assessment of the pump twin showed normal morphology with no evidence of cardiac dysfunction. The presentation was cephalic, 33 weeks by biparietal diameter, 29 4/7weeks by femoral length. Sonographic estimated fetal weight was 2,149 to 2,180 grams, appropriate for gestational age. Surveillance of the pump twin was reassuring. Biophysical profile scores remained 10/10 on serial testing. Doppler velocimetry studies showed normal indices for the right uterine artery and the umbilical artery. The indices of the left uterine artery were elevated with end-diastolic notching. The acardiac twin, on the other hand, was malformed. It appeared on sonography like a solid egg-shaped mass with a single malformed lower extremity protruding from it. The central mass showed a slit-like midline defect which was initially thought to be an open neural tube defect. This defect was flanked on either side by dimplings. Estimated weight was 152.4 grams. Umbilical artery pulsatility index was elevated at 2.63 with absent diastolic flow. The acardiac twin progressively grew in size. At 35 weeks age of gestation, amniocentesis showed immature fetal lungs, hence intramuscular dexamethasone 6 mg at 12-hour intervals for four doses was administered. Fetal 2D echocardiography done at 36 weeks age of gestation confirmed normal cardiac structure and function of the pump twin.

At 37 weeks age of gestation a live morphologically normal baby girl, weighing 2,500 grams, appropriate for age, 38 weeks by pediatric age, APGAR score of 9 remaining 9 was delivered via repeat low segment cesarean section. The baby was directly roomed-in with the mother and was discharged well (Figure 3A). The acardiac twin weighed

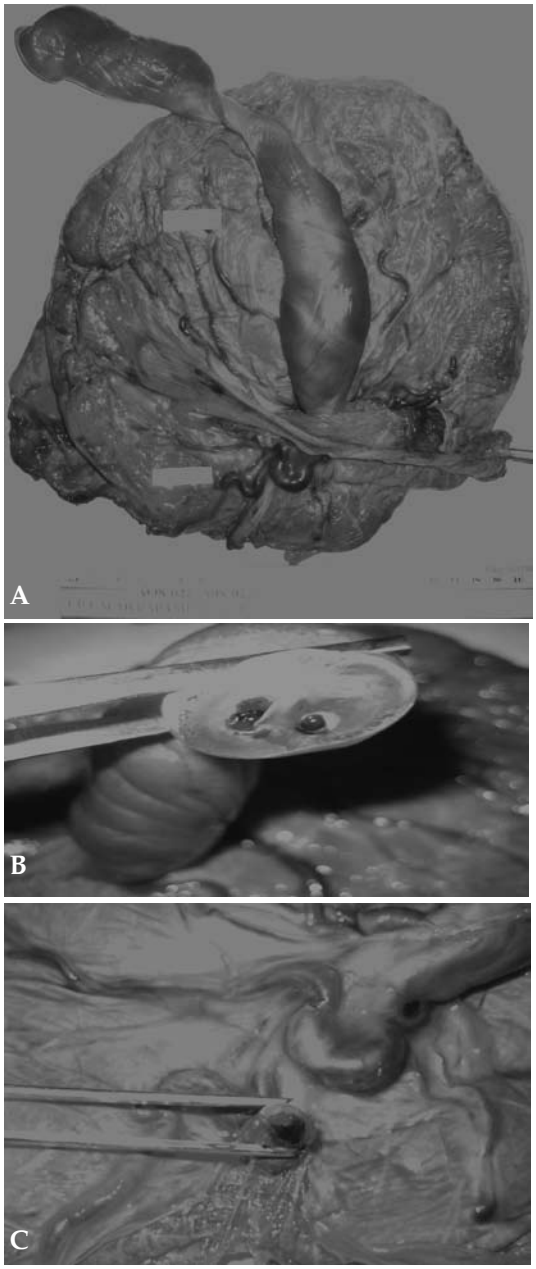

Figure 2. The placenta was monochorionic, monoamnionic, weighing 600 grams, with several superficial arterio-arterial and veno-venous anastomoses. The umbilical cord of twin A had three vessels and was edematous while that of twin B had two vessels.

1,200 grams. It consisted of a head with a mouth from which a tongue protruded and a single lower extremity with four toes. Provisional autopsy revealed a chorangiopagus parasiticus twin, acardius anceps amorphous type, weighing 1,250 grams, 26 weeks by morphometry with the following: amorphous internal organs, omphalocele, imperforate anus, absent external genitalia, deformed cranial vault, undeveloped diaphragm, ascitis (29 ml.), anasarca, and a single lower extremity with oligodactyly (Figure 3B & C). The placenta was monochorionic, monoamnionic weighing 520 grams with demonstrable artery to artery and vein to

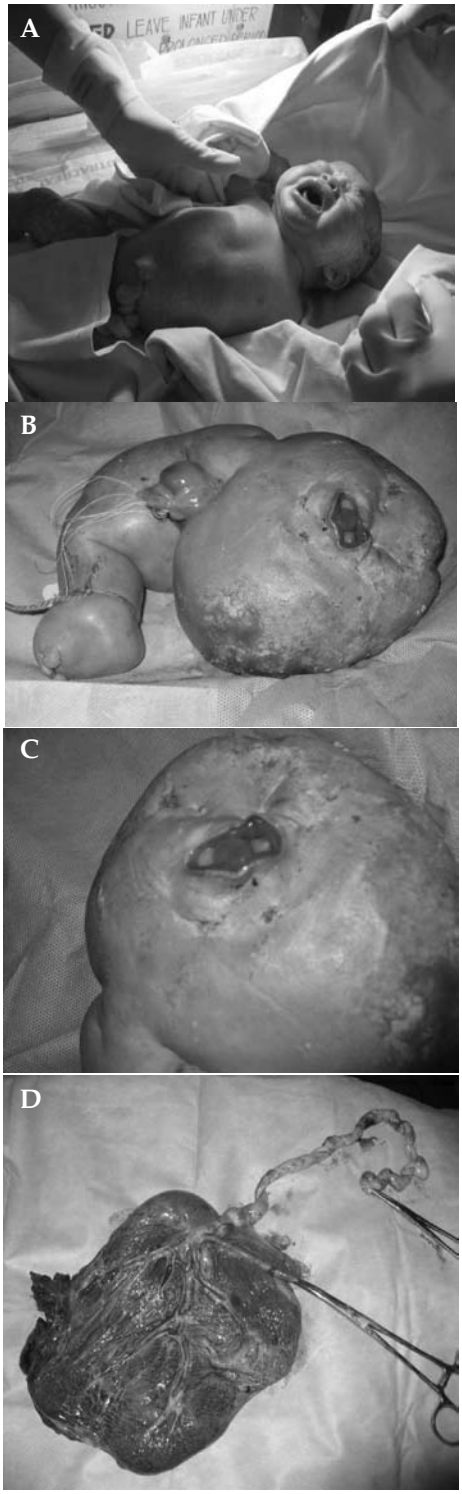

Figure 3. A, Live baby girl, 38 weeks pediatric aging, morphologically normal, weighing 2,500 grams, APGAR 9-9 B & C, Acardius anceps amorphous type, weighing 1,250 grams, 26 weeks by morphometry, amorphous internal organs, omphalocele, imperforate anus, absent external genitalia, deformed cranial vault, undeveloped diaphragm, ascitis (29 ml.) and anasarca, and single lower extremity with oligodactyly. D, Monochorionic, monoamnionic placenta,weighing 520 grams with artery to artery and vein to vein anastomosis. The umbilical cord of the normal pump twin was trivesseled while that of the acardiac twin was two-vesseled. (with permission)

vein anastomoses. The umbilical cord of the normal pump twin had three vessels while that of the acardiac twin had two vessels (Figure 3D).

Discussion

The primary cause of the developmental abnormalities has not been fully elucidated. There are two major theories. The first is that the embryo or fetus is primarily abnormal and is kept alive by vascular communications between it and the normal co-twin. The second theory is that it results from a reversed circulation and hypoperfusion. The latter theory, twin reversed-arterial perfusion sequence, is the most widely accepted theory on the pathogenesis of acardius. In TRAP sequence, all organs of the recipient twin may be affected with varying degrees of severity. Giménez-Scherer and Davies studied the malformations found in acardiac twins and dysmorphic twins with absent or rudimentary hearts excluding amorphous masses without head-tail orientation. The objective was to determine whether the malformations occurred randomly or in a pattern related to the twinning process. They tabulated alterations in the organs and long bones according to the embryonal-fetal circulation of blood from and to the placenta. They found that malformations were more often encountered in the superior limbs and organs and that the number of altered organs decreased in a cranio-caudal direction except for the liver. The liver, which lies first in the circulatory path from placenta to the fetus, was affected in 89% of cases compared with other abdominal organs which were affected on an average of 54%. The pattern of the malformations is compatible with the TRAP sequence. The more frequent absence of distal bones is compatible with reduced perfusion in each limb. The malformations found in acardiac twins involved brain, esophagus and trachea, liver, other abdominal organs, diaphragm, vertebrae, limbs, anus and omphalocoele. Vascular disruption may be the common pathogenesis for acardiac twins.[9] Demonstration of retrograde perfusion by color flow Doppler confirms the diagnosis of TRAP sequence. Visualization of cardiac activity in the recipient twin does not exclude the diagnosis since a rudimentary heart may be present. [4]

The first theory, a lethal defect in early development with "rescue" of the circulation by the normal co-twin, would present a normally directed blood flow and malformations would not have an increasing severity in a caudal-cranial direction with special emphasis on the liver. Furthermore, there are no reports of acardiacs with an artery to vein transfusion and a normally directed circulation from the co-twin.[9]

A chromosomal anomaly as a mechanism of absence of the heart has also been suggested. Chromosomal anomaly, however, does not explain the reversed circulation and the peculiar cranio-caudal distribution of the other malformations in these fetuses, features that are also found in fetuses with normal karyotype, and in fetuses with similar karyotypes as their co-twin.[9] TRAP sequence is a

more plausible explanation.

Chorangiopagus parasiticus is a term coined by Schwalbe in 1906-1907 that refers to the acardiac twin. Table 1 shows the classification and distribution of the various forms. Acardius acormus is the rarest form. The term is used for forms with a head but without the rest of the body. The head may be attached directly to the placenta. An acardius amorphous is a mass of bone, muscle, fat and connective tissue without any recognizable human form and is connected by the umbilical cord to the placenta. Acardius acephalus is the most commonly encountered variant. It is characterized by absence of the head, upper limbs, pectoral girdle and thoracic organs. The lower limbs, genitalia and abdominal viscera persist. In acardius anceps a rudimentary cranial structure is present and there is persistence of limbs and other organs. A rudimentary heart may be present.[2,8,10,11] The acardiac twin in the first new case presented (case 1) was an acardius acephalus. The head, thorax, upper extremities and some of the abdominal organs, specifically the esophagus, stomach, liver, pancreas and gallbladder, were absent. Both lower extremities were present with malformed feet. The acardiac in the second case (case 2), on the other hand, was an acardius anceps, amorphous type. There was a deformed cranial vault and a single deformed lower extremity. The internal organs were amorphous.

Table 1. Classification and distribution of chorangiopagus parasiticus (CAPP) twins[8]

Expanded Classification	Percent	Simplified classification
Acardius holosomus	14.7%	Acardius anceps
Holocranius	12.5%	
Hemicranius	2.3%	
Acardius Hemisomus	68.0%	Acardius acephalus
Acephalus	10.2%	
Holocranius	3.4%	
Hemicranius	6.8%	
Acranius	35.2%	
Athorax	6.8%	
Arrachis	3.4%	
Acormus	2.2%	Acardius acormus
Incompletus	1.1%	
Completus	1.1%	
Acardius amorphous	17.0%	
Externus	8.0%	Acardius myelocephalus
Totalis	9.1%	Acardius amorphous

SOURCE: Severn CB and Holyoke EA. Human Acardiac anomalies. Am J Obstet Gynecol. 1974;11(3):358-365.

The placental morphology in both case 1 and case 2 were similar. Both placentas were single monochorionic-monoamnionic placentas, with three-vessel umbilical cords attached to the normal co-twins and two-vessel umbilical cords supplying the acardiac twins. In both placentas, arterio-arterial and veno-venous placental anastomoses were documented. In addition, in each placenta, the placental insertion site of the umbilical cords were located close to each other. In case 1, the umbilical cord of the pump twin was markedly edematous. Two-vessel umbilical cord and cord insertion close to the cord of the pump twin are common findings in acardiac twinning.

Ultrasound imaging is currently the standard method of diagnosing acardiac twinning and TRAP sequence. Doppler ultrasound imaging is crucial in the identification of retrograde perfusion in the recipient/acardiac twin and in its umbilical artery. Doppler ultrasound imaging is used to locate arterio-arterial and veno-venous anastomoses in the placenta to strengthen the diagnosis or during surgical interventions. Non-gated fetal MRI is being investigated as an adjunct to Doppler ultrasound imaging in examining arterial blood flow within the acardiac twin.[12] Ultrasound findings consistent with TRAP sequence would include the following: monochorionic placenta; amniotic fluid abnormalities especially polyhydramnios around the pump twin, and dysmorphic recipient twin. The sonographic appearance of the recipient twin varies widely depending on the body parts or organs involved and severity of alteration-reduction/malformation (see classification of chorangiopagus parasiticus). Appearance may range from a formless structure to a headless fetus or one with a small head and brain malformations. Generally, the cephalic pole of the fetus is more severely affected than the podalic pole-consistent with the retrograde flow in the umbilical artery into the recipient fetus. On sonography excessive soft tissue echoes, diffuse subcutaneous edema, bizarre skeletal echoes and cystic spaces may be seen. In complete cardiac agenesis cardiac motion is absent. Visualization of cardiac activity in the recipient twin does not exclude the diagnosis since a rudimentary heart may be present. Demonstration of retrograde perfusion by color flow Doppler confirms the diagnosis of TRAP sequence. Retrograde perfusion was demonstrated on color flow Doppler in case 2. Unfortunately, the presence of retrograde flow was not investigated in case 1 nor was a search/imaging of placental vascular anastomosis by means of color Doppler attempted in both cases.

TRAP sequence is a heterogeneous condition with variable expression of risk factors for poor pregnancy outcome. In a significant number of cases the acardiac twin is smaller than the pump twin. In such circumstances, the pump twin may not show evidence of cardiac dysfunction (secondary to the increased hemodynamic demand of the systemic shunt) and will have a favorable perinatal outcome without the need for antenatal interventions.[13] Moore and colleagues reported that the weight of the acardiac twin has bearing on the survival of the pump twin. When the weight of the acardiac twin expressed as a percentage of the pump twin's weight is >70%, 50 to 70%, and <50%, the risk of congestive heart failure in the pump twin is 100%, 70%, and 8%, respectively. There is a higher likelihood of polyhydramnios or hydrops with a higher (>50%) TRAP twin to pump twin birthweight ratio.[3,14,15] The intrauterine volume is increased by polyhydramnios and/or the progressive enlargement of the hydropic acardiac

twin. This predisposes to premature labor and delivery.[15] In the first case presented, the acardiac to pump twin weight ratio was determined antenatally by ultrasound. The twin weight ratio was 50%. The twin birthweight ratio, however, was greater at 142.86%. Sonographic estimation of fetal weight is inaccurate or has great variability. The marked discrepancy in weight ratio may also be due to an increase in edema in the acardiac twin.

Predictors of poor prognosis for the pump twin are the development of polyhydramnios, cardiomegaly, pericardial effusion, tricuspid regurgitation, reversed flow in the ductus venosus, pulsations in the umbilical vein and signs of anemia. The following predictors of poor prognosis were present in case 1: a high acardiac to pump twin weight ratio, polyhydramnios, cardiomegaly and mild pericardial effusion.

The pregnancy outcome was an intrauterine fetal death at less than 33 weeks gestation. None of the predictors were present in the second case. The acardiac to pump twin birthweight ratio was 48%. There was neither cardiac dysfunction (no cardiomegaly) nor amniotic fluid abnormality. The absence of risk factors enabled the pregnancy to reach term and produce a good neonatal outcome—a live birth with a good APGAR score and adequate birthweight.

Dashe et al. studied Doppler velocimetric findings in six twin pregnancies complicated by TRAP sequence. They observed that larger differences in resistive index between the pump and acardiac twin (>0.20) was associated with improved outcome of the pump twin while smaller resistive index differences (<0.05) were associated with poor outcome including cardiac failure and central nervous system hypoperfusion. Additional observations were: five of the six acardiac twins had elevated Doppler index values; and no association could be observed between outcome and a particular systolic to diastolic flow ratio value or resistive index value of the umbilical artery of the acardiac twin alone. According to Dashe et al., a small difference in umbilical artery flows between the twins, represented by a small difference in Doppler index values, suggests a relatively large artery-to-artery placental communication providing the acardiac twin a great deal of blood flow from the pump twin, thus portending a poor prognosis. In contrast, a large difference in Doppler index values between the twins might mean less flow supplying the acardiac twin thus, less likelihood of the pump twin developing high output failure.

The study has limitations. The sample size was small precluding determination of statistical significance, but then TRAP sequence is rare. Doppler indices were obtained at a variety of gestational ages (second trimester till delivery). Further studies are needed to determine whether differences in resistive indices obtained early in gestation are predictive of the pregnancy outcome at a later date.[2]

A rapidly growing severely hydropic acardiac twin and signs of cardiac compromise in the pump twin signal the need for intervention. A variety of surgical modalities aimed at curtailing circulation to the acardiac twin have been employed, such as: hysterotomy with selective delivery of the acardiac twin; extrafetal-extravascular techniques (e.g., 1.6- to 3.8-mm port, ultrasound or endoscope guided ligation with or without transection of the acardiac twin's umbilical cord, laser coagulation of the umbilical cord of the acardiac twin or of the arterio-arterial and/or veno-venous placental vessel anastomosis or bipolar electrocautry); extrafetal-intravascular techniques (e.g., 22-gauge needle, ultrasound guided funicular alcohol injection, funicular helical coil insertion); intrafetal-extravascular techniques (e.g., 18-gauge to 3-mm port, ultrasound guided radiofrequency ablation, laser or monopolar electrocautery), and; intrafetal-intavascular techniques (e.g., 18-22-gauge needle, ultrasound guided alcohol injection, monopolar electrocautery or laser). Most investigators agree on the criteria for offering surgical interventions but the optimal surgical approach or specific technique that would provide the best outcome has not been defined.[3] Endoscopic techniques are lengthier procedures, more invasive and more cumbersome than ultrasound guided needle techniques. Endoscope assisted umbilical cord occlusion requires specialized equipment and highly skilled operators, both of which are only available in a few centers in the world. In addition, it may be complicated by the need for a second port for amnioinfusion or for septostomy. Four methods of ultrasound guided intrafetal ablation are: intravascular chemosclerosis with absolute alcohol; monopolar diathermy; interstitial laser ablation, and radiofrequency ablation.[16] Tan and Supleveda systematically reviewed 71 cases of TRAP sequence comparing the different treatment modalities (classified into cord occlusion by ultrasound, by endoscopy, or by intrafetal access) and their outcome. They found that intrafetal ablation was associated with a higher gestational age at delivery (37 weeks vs 32 weeks), a higher median treatment to delivery interval (16 vs 9.5 weeks), a lower technical failure rate (13% vs 35%), and a lower rate of premature delivery or rupture of membranes before 32 weeks gestation (23% vs 58%) compared with cord occlusion techniques.[17] Intrafetal techniques had an 84% survival rate compared with 67% for ultrasound guided techniques or 72% of endoscopic procedures.[3,17] Supelveda et al. suggested an inexpensive, rapid, less invasive alternative to endoscope assisted procedures. They had good experience with percutaneous intrafetal intravascular alcohol injection for eradication of the circulation to the acardiac twin. It entailed mere insertion under ultrasound and/or Doppler guidance of a 20-gauge spinal needle into the intraabdominal segment of the umbilical artery and injection of approximately 2 ml of absolute alcohol into the vessel. Absolute alcohol acts as a vascular sclerosant. The procedure was followed by amniodrainage to address polyhydramnios which often accompanies acardiac twinning.[13] Denbow et al. advised against intravascular injection of alcohol for umbilical vessel occlusion.[13] It was pointed out by Quintero et al. that several

cases using intrafetal alcohol injection wherein the pump twin died were not included in the review of Supelveda. Furthermore, Ozeren et al. subsequently reported a case where death of the pump twin occurred after a failed intrafetal alcohol injection.[3]

The timing of intervention seems important. In a recent series of cord coagulation in complicated monochorionic multiple pregnancies, it was found that interventions done at advanced gestational ages or when cardiac compromise has already set in correlated with mental delay and unfavorable neurologic outcome in the surviving pump twin.[18]

In TRAP sequence, the recipient twin has a lethal malformation (acardia or acephaly). Management of TRAP sequence therefore, focuses on the pump twin and aims to optimize conditions to ensure survival of the pump twin. Early recognition of the condition is crucial. Close fetal surveillance using ultrasound and Doppler ultrasound imaging is necessary to detect risk factors for poor outcome such as polyhydramnios, hydrops, cardiac decompensation of the pump twin, high twin weight ratio, rapid enlargement of the acardiac twin, fetal growth restriction and abnormal Doppler flow indices. Care of such a high risk pregnancy necessitates a multidisciplinary team composed of an obstetrician, perinatologist, pediatrician, neonatologist, pediatric cardiologist and individuals skilled in intrafetal surgery or semi-invasive procedures.

In the Philippine setting, expectant management is done especially in the absence of risk factors. Close fetal surveillance in the form of congenital anomaly screening, fetal echocardiography, Doppler velocimetry studies, serial biometry, biophysical profile and non-stress testing are done. Steroids are given to hasten pulmonary maturity. When risk factors for poor prognosis set in, the multidisciplinary team has limited options. Polyhydramnios may be managed by serial amnioreduction and/or indomethacin. Digoxin may be given to the mother for early fetal cardiac dysfunction. The specialized equipment and highly skilled operators required for endoscopic or fetoscopic interventions are not available at this point in time. Semi-invasive techniques involving ultrasound- or Doppler imaging-guided needle insertions are feasible in this setting but experience is limited. Intravascular alcohol injection is fitting for tertiary hospitals such as the Philippine General Hospital which caters more to individuals from the lower socio-economic group, and where endoscopic equipment and operators skilled in intrauterine fetal surgery are not readily available at the moment. However, studies show a high failure rate with this procedure. An intervention must be evaluated for efficacy and safety preferably by randomized controlled trials before it can be recommended for use. However, evaluation is difficult since TRAP sequence with acardiac twinning is rare and the presentation heterogeneous. In the first case presented, maternal digitalization was done. Digoxin crosses the placenta and hopefully provides inotropic support for the failing heart of the pump twin. Amnioreduction was contemplated. Unfortunately, demise of the pump twin occurred before amnioreduction could be performed.

Counseling is an integral part in management especially when congenital anomalies are detected. Often, the family history does not reveal a risk factor nor a previous occurrence in the family. The couple must be told that no maternal condition predisposes to the acardius phenomena. No recurrence has been reported. Routine cytogenetic investigation is suggested by Blaicher in order to evaluate the impact of aneuploidy in acardiac twin pregnancies. Several investigators found karyotypes in the acardiac twin different from those in the co-twin (Benirschke and Kaufmann 1995).[19] Cytogenetic studies were not performed in any of the cases presented.

Management of TRAP sequence must be tailored to the clinical presentation, the capabilities for surveillance and treatment within the medical institution or facility and the prevailing practice in the geographic location.

References

1. Arias F, Sunderji S, Gimpelson R, Colton E. Tre!tment of Acardiac Twinning. Obstet Gyn.1998;91:818-21.
2. Dashe J, Fernandez C and Twickler D. Utility of Doppler velocimetry in predicting outcome in twin reversed-arterial perfusion sequence. American Journal of Obstetrics and Gynecology. 2001;185(1).
3. Quintero R, Chmait R, Murakoshi T, et al. Surgical management of twin reversed arterial perfusion sequence. American Journal of Obstetrics and Gynecology. 2006;194:982-91.
4. Diehl W, Hecher K. Selective Cord Coagulation in Acardiac Twins. Seminars in Fetal and Neonatal Medicine. 2007; 12:458-463.
5. Healey MG. Acardia: predictive risk factors for the co-twIn's surviva,. Teratology. 199 ;50:205-13.
6. Chen CC, Hsu YH, Chan TF, Yuan SS, Su JH. Poor Long- Term Outcomes in a Survivor preSenting with Twin-Reversed-Arterial-Perfusion SequEnce In UterO: A case report. Kaohsiung J Med Sci. Oct. 2003;19:526-30.
7. Acosta–Sison H, Aragon GT and De la Paz A. Mono-amniotic twins: Danger to the life of at least one twin (First case report in the Philippines). J Philip Med Assoc. 1946;22:(2):44–46.
8. Ramos-Costa CJ, Tansengco L. "When heart beats are shared…" A case of acardiac twinning. Philippine Journal of Obstetrics and Gynecology. 2004;28(2):80-85.
9. Giménez-Scherer JA, Davies B. Malformations in acardiac twins are consistent with reversed blood flow: Liver as a clue to their pathogenesis. Pediatric and developmental Pathology. 2003;6:520-530.
10. Severn CB, Holyoke EA. Human Acardiac anomalies. Am J Obstet Gynecol. 1974;11(3):358-365
11. Bonella-Musoles F, Machado LE, Raga F, Osborne NG. Fetus Acardius: two-and three- dimensional ultrasonographic diagnosis. J Ultrasound Med. 2001; 20:1117-1127.
12. Hata N, Wada T, Kashima K, et al. Non-gated fetal MRI of umbilical blood flow in acardiac twin. Pediatr Radiol. 2005;35:826-829.
13. Sepulveda W, Sfier D, Reyes M. and Martinez J. Severe polyhydramnios in twin-reVersed-arterial-perfusion sequence: successful management with intrafetal alcohol ablation of acardiac twin and amniodrainage. Ultrasound Obstet Gynecol. 2000;16:260-263.
14. Moore TR, Gale R, Benirshke G. Perinatal outcome of 49 pregnancies complicated by acardia. Am J Obstet Gynecol. 1990;163(3):907-912.
15. Hecher K, Hackeloer BJ, Ville Y. Umbilical cord coagulation by operative microendoscopy at 16 weeks gestation in an acardiac twin. Ultrasound Obstet Gynecol. 1997;10:130-132.
16. Sepulveda W, Hasbun J, Dezerega V, Devoto J and Alcalde J. Successful sonographically guided laser ablation of a large acardiac twin at 26 weeks gestation. J Ultrasound Med. 2004;23;1663-1666.
17. Tan TYT, Supelveda W. Acardiac Twins: a systematic review of minimally invasive treatment modalities. Ultrasound Obstet Gynecol. 2003; 22: 409-19.
18. Lewi L, Gratacos E, Ortibus E, et al. Pregnancy and infant outcome of 80 consecutive cord coagulations in complicated monochorionic multiple pregnancies. Am J Obstet Gyncol. 2006;194:782-9.
19. Blaicher W, Repa C, Schaller A. Acardiac twin pregnancy: associated with trisomy 2. Human Reproduction. 2000;15(2):474-475.