Perinatal outcome of forty-nine pregnancies complicated by acardiac twinning

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Abstract

Acardiac twinning affects 1 in 100 monozygotic twin pregnancies and 1 in 35,000 pregnancies overall. The presence of an acadiac twin requires the normal (or "pump") twin to provide circulation for itself, as well as the acardiac sibling. In many cases the acardiac twin is almost equal to the normal twin. The principal perinatal problems associated with acardiac twinning are pump-twin congestive heart failure, maternal hydramnios, and preterm delivery. We reviewed the perinatal courses of 49 acardiac twin pregnancies to identify factors prognostic of favorable outcome. The overall perinatal mortality was 55%, primarily associated with prematurity. Mean (+/- SD) gestational age at delivery was 29 +/- 7.3 weeks, with a mean (+/- SD) normal twin weight of 1378 +/- 1047 gm. The acardiac weight averaged 651 +/- 571 gm. However, the occurrence of hydramnios, the occurrence of preterm labor, and perinatal outcome were strongly related to the ratio of the acardiac and pump-twin's weight. The mean overall ratio of the twin weights was 52% +/- 42%. However, the mean weight ratio for patients delivered before 34 weeks was 60% versus 29% (p less than 0.04). Preterm delivery was strongly associated with the development of hydramnios and congestive heart failure in the pump twin (p less than 0.01). If the twin-weight ratio was above 70% (25% of cases), the incidence of preterm delivery was 90%; hydramnios, 40%; and pump-twin congestive heart failure, 30% compared with 75%, 30%, and 10%, respectively, when the ratio was less (p less than 0.05). Regression of the weight of the acardiac twin against its longest dimension (L) resulted in this equation for prediction of acardiac weight: Weight (grams) = 1.2 L²-1.7L; r = 0.79, p less than 0.01. These data suggest that estimation of the relative weights in acardiac twins provides prognostic information regarding outcome. Poor outcome occurs with congestive heart failure and hydramnios in the normal twin. Use of the above data may assist in counseling patients and determining optimal management.
Perinatal Outcome of Conservative Management versus Fetal Intervention for Twin Reversed Arterial Perfusion Sequence with a Small Acardiac Twin

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Abstract

\textbf{Objective:} To examine the outcomes of patients with twin reversed arterial perfusion (TRAP) sequence in which the acardiac twin was $\leq 50\%$ the weight of the pump twin.

\textbf{Methods:} This was a retrospective study conducted with institutional review board approval. The records of all patients referred to UCSF for suspected diagnosis of TRAP between 1994 and 2009 were reviewed ($n = 76$). Patients with pregnancies complicated by TRAP with an acardiac twin $\leq 50\%$ the weight of the pump twin were included (21 patients). Exclusion criteria were loss to follow-up (1 patient) and syndromic abnormalities in the pump twin (2 patients).

\textbf{Results:} Of the 18 patients with viable pregnancies that met the criteria for analysis, 7 (39\%) underwent radiofrequency ablation (RFA) of the acardiac twin and 11 (61\%) underwent conservative management. None of the pump twins in either group had hydrops fetalis. Three of the 11 acardiac twins in the conservative management group did not undergo RFA because they did not have blood flow at presentation to UCSF. Survival to delivery was 100\% (7/7) in the RFA group and 91\% (10/11) in the conservative management group.

When we eliminated from our analysis the 3 pregnancies in the conservative management group without blood flow to the acardiac twin, survival to delivery was 88\% (7/8). The single death occurred in 1 of the 3 monochorionic-monoamnionic pregnancies in the conservative management group, all of whom had blood flow to the acardiac twin. There were no statistically significant differences in gestational age at delivery, birth weight or survival between the RFA and conservative management groups, even after stratification by blood flow.

\textbf{Conclusions:} Conservative management with close monitoring appears to be a safe option for TRAP pregnancies in which the acardiac twin is $\leq 50\%$ the weight of the pump twin.

Introduction

Twin reversed arterial perfusion (TRAP) sequence is a disorder of monochorionic twins in which one of the twins has a nonfunctioning or absent heart and receives all of its perfusion from its co-twin. The acardiac twin has no placental share, and perfusion occurs through an arterial-arterial connection between the structurally normal pump twin and the acardiac twin. Blood flows into the acardiac twin retrograde through the umbilical ar-
Acardiac twin

Andrew Murphy and Dr Yuranga Weerakkody et al.

Acardiac twins (or recipient twins) are haemodynamically disadvantaged non-viable twins that undergo secondary atrophy in association with a twin reversed arterial perfusion sequence.

Epidemiology

Acardiac twinning is thought to affect 1 in 100 monozygotic twin pregnancies and 1 in 35,000 pregnancies overall. There is no recognised familial recurrence.

Pathology

The acardiac twin undergoes secondary atrophy of the heart and dependent organs (brain) and often develops a characteristic set of anomalies including acardia and acephalus. This twin exerts abnormal strain on the opposite (pump) twin by stealing its circulation.

There are two schools of thought in the pathogenesis of the acardiac twin:

- some propose that the primary defect is one of cardiac embryogenesis (dysmorphogenesis)
- others consider the primary cause being an abnormal vascular communication between embryos in the placenta with arterial to arterial communication leading to reversed flow of blood to the haemodynamically disadvantaged or recipient twin, with resulting secondary atrophy of the heart and dependent organs.

Subtypes

An acardiac twin can present with four morphological types:

- **acardius anephus**
  - most common type
  - there is an absence of the head and upper torso and limbs in the acardiac twin with preservation of the lower limbs, genitalia and abdominal viscera

- **acardius anceps**
  - most developed type
  - rudimentary cranial structures present with otherwise persistent trunk, limbs and organs
  - however lacks even a rudimentary heart

- **acardius amorphus**
  - least differentiated type
  - comprises of an amorphous mass of bone, muscle, fat and connective tissue
  - if rudimentary nerve tissue is present, it is then called acardius myelantencephalus

- **acardius acormus**
  - rarest type
  - the only developed structure is the fetal head
  - all other structures are essentially absent
the umbilical cord insertion is directly into the fetal head
pathologically rudiments of thoracic structures may be present

Associations

- **single umbilical artery**: ~66%
- underlying **chromosomal anomaly**: ~33%

Radiographic features

**Ultrasound**

While features can vary with each subtype, general features include

- **fetal biometric discordance**
- marked edema (**fetal anasarca**) of the affected twin with cystic changes
- normal or accelerated growth of the lower extremities due to an imbalance in the interfetal circulation.
- retrograde supply of the desaturated blood to the upper body and head leads to maldevelopment of the heart, head, and upper torso, which are completely absent or severely deficient
- the umbilical cord to the acardiac twin is often quite short and may be difficult to identify

**Doppler assessment**

Shows reversed flow through the umbilical arteries to the affected fetus.

Complications

The other donor (pump) twin may develop cardiac failure (**hydrops**) with a reported mortality of 50-75%.

**Treatment and prognosis**

The acardiac twin is non-viable and management is aimed at maintaining the viability of the other (donor/pump) twin, including close surveillance for development of hydrops. Interrupting blood flow to the acardiac twin may be performed by various methods which include hysterotomy and removal of the acardiac twin, ligation of the umbilical cord and/or laser ablation of vessels.

References

INTRODUCTION

Twin reversed arterial perfusion sequence (TRAP) refers to a rare, unique complication of monochorionic twin pregnancy in which a twin with an absent or a nonfunctioning heart ("acardiac twin") is perfused by its co-twin ("pump twin") via placental arterial anastomoses. The acardiac twin usually has a poorly developed heart, upper body, and head. The pump twin is at risk of heart failure and problems related to preterm birth.

INCIDENCE

TRAP sequence has historically been reported to occur in about 1 percent of monochorionic twin pregnancies and 1 in 35,000 pregnancies [1]. These figures are widely cited but based on data available up to 1953. In contemporary obstetrics, the incidence appears to be much higher when factors such as the use of first trimester obstetric ultrasound examination, which detects twin demises early in gestation, and assisted reproductive techniques, which have increased the incidence of twins including monochorionic twins, are accounted for. A 2015 study estimated the incidence of acardiac twins is 2.6 percent of monochorionic twin pregnancies and 1 in 9500 to 11,000 pregnancies [2].

PATHOPHYSIOLOGY

In the normal fetal circulation, blood from the placenta flows through the umbilical vein to the fetus. From there, the ductus venosus shunts 80 percent of the placental blood flow into the inferior vena cava, where it mixes with venous return from the lower extremities and kidneys before entering the right atrium (figure 1). Once the blood enters the right atrium, the two sides of the fetal heart act in parallel through intra- and extra-cardiac shunts (foramen ovale, ductus arteriosus) to fill the aorta and provide systemic circulation. The distal aorta terminates in the left and right common iliac arteries, which each divide into internal and external iliac branches. The umbilical arteries carry blood from the internal iliac arteries back to the placenta.

In TRAP sequence, the pump twin maintains this normal pattern of fetal circulation. In addition, a portion of its cardiac output travels through placental arterial-arterial anastomoses to the umbilical artery and eventually the systemic circulation of the recipient co-twin, thus creating "reversed" circulation in this twin. This is possible because the acardiac twin lacks a functional heart, whose pumping would normally provide forward flow and high systemic pressure. The presence of arterial-arterial anastomoses allows blood to be pumped from the normal twin to the acardiac twin without passing through a capillary bed.
Veno-venous and arterio-venous anastomoses also occur. The presence of placental vascular anastomoses is common in monochorionic twins and alone is not sufficient for the development of TRAP sequence. The abnormal circulatory pattern provides perfusion of deoxygenated blood from the pump twin to the lower half of the recipient twin via its iliac arteries, but poor perfusion of the upper torso and head. Unequal vascular perfusion from the pump twin may contribute to the evolution of a variety of structural abnormalities in the recipient twin [3].

References

The management of acardiac twins: A conservative approach

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OBJECTIVE: Optimal management of acardiac twin pregnancies is controversial. Data suggest a 50% mortality rate in the “pump” twin when the pregnancy is managed expectantly. Because of increased antenatal diagnosis, outcomes in expectantly managed cases may be better than reported. Our objective was to determine the outcome of expectantly managed acardiac twin pregnancies.

STUDY DESIGN: All cases of antenatally diagnosed acardiac twins delivered in our community between 1994 and 2001 were ascertained. All were managed expectantly. Perinatal outcome of pump twins was the primary outcome variable.

RESULTS: Ten cases were identified. Nine women were delivered of healthy pump twins. There was one neonatal death. The mean gestational age at delivery was 34.2 weeks. The mean weights of the pump and acardiac twins were 2279 g and 1372 g, respectively.

CONCLUSION: Neonatal mortality of pump twins in antenatally diagnosed acardiac twin pregnancies may be considerably less than reported. Expectant management with close antepartum surveillance deserves consideration. (Am J Obstet Gynecol 2003;189:1310-3.)

Key words: Acardiac twins, TRAP sequence

The twin reversed arterial perfusion (TRAP) sequence, also known as acardiac twinning, is a rare obstetric condition unique to monochorionic twin gestations. This condition complicates approximately 1 of 35,000 pregnancies and occurs in 1% of monochorionic twin gestations.1,2 The TRAP sequence involves a “pump” or donor twin perfusing a recipient or “acardiac” twin through vascular (usually arterial-arterial) anastamoses. This results in reversed flow of poorly oxygenated blood through the recipient twin that is usually associated with poor or absent development of the heart, hence the term acardiac.

The reported fetal/neonatal mortality of the “pump” twin is extremely high (50%-75%)2,6 and is thought primarily to be due to increased cardiac demands on the pump twin in an effort to perfuse its acardiac sibling. The high mortality rate has prompted most authorities to advise the antepartum use of invasive procedures intended to disrupt the blood flow from the pump twin to the acardiac recipient. Such procedures include hysterotomy with selective delivery of the acardiac twin, and umbilical cord occlusion of the acardiac twin with the use of a variety of techniques through laparoscopy, fetoscopy, or ultrasound guidance.

In addition, reported mortality rates for pump twins may be overestimated because they are based primarily on cases ascertained at the time of delivery or autopsy. Also, most studies were conducted in tertiary care centers and are limited to referral cases. As such, published series are likely biased toward the most severe cases with the worst perinatal outcomes. Our purpose was to determine the outcome of acardiac twin pregnancies that were diagnosed antenatally and managed expectantly.

Methods
This was an observational study of all cases of antenatally diagnosed acardiac twin pregnancies delivered in our community between January 1994 and August 2001. Cases were ascertained by searches of medical records by use of International Classification of Diseases, 9th Revision, codes and databases of all of the perinatal centers in Utah for acardiac twins. Each patient was seen by a maternal-fetal medicine specialist, although many
Treatment of acardiac twinning.

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Abstract

BACKGROUND:
The twin reversed-arterial-perfusion sequence is a complication of monochorionic twin pregnancies characterized by the hemodynamic dependence of a "recipient" twin from a "pump" twin. The recipient twin exhibits lethal abnormalities including acardia and acephaly. The pump twin has a mortality rate of 50% as a result of high-output heart failure.

CASE:
The blood supply to an acardiac-acephalus twin was interrupted at 24 weeks' gestation using endoscopic laser coagulation. The co-twin was delivered at 35 weeks and had an uneventful neonatal course following correction of a persistent patent ductus arteriosus. Review of the literature reveals 22 cases of acardiac twinning treated with invasive procedures, seven of them using endoscopic laser coagulation. Pump twin mortality with fetal surgery was 13.6% in comparison with 50% mortality with expectant management (P < .001).

CONCLUSION:
Fetal surgery is the best available treatment for acardiac twinning. Endoscopic laser coagulation at or before 24 weeks and endoscopic or sonographic guided umbilical cord ligation after this gestational age seem to be the best treatments for this condition.
First trimester diagnosis of acardiac twins

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Abstract

OBJECTIVE: To describe ultrasonographic findings from 5 to 17 weeks of gestation in monozygotic twin pregnancy resulting in acardia of one twin.

METHODS: Transvaginal ultrasonographic examinations were performed using a 7.5 MHz probe at weekly intervals from week 5-11. Uterine artery PI were measured using color Doppler flow. Embryonic heart rates were determined with M-mode.

RESULTS: A monochorionic gestational sac containing 2 embryos demonstrated embryonic cardiac activity between 5 and 7 weeks. One twin lost cardiac activity at 7 weeks. A diagnosis of acardiac twins was made at 1 weeks when growth of the lower extremities and no development above the thorax as well as reversal of blood flow through the umbilical cord of the acardiac twin was noted by 14 weeks.

CONCLUSION: Ultrasonographic demonstration of independent embryonic heart rates from 5-6 weeks and reversal of blood flow through the umbilical cord of the acardiac twin suggest that the primary pathogenesis in acardia is cardiac dysmorphogenesis secondary to reversal of blood flow rather than primary cardiac agenesis. Acardiac twins can spontaneously ligate connection with their viable twin. Acardiac twinning is a rare complication of multifetal gestation occurring in 1% of monozygotic twin pregnancies or 1 in 35000 births (1). Acardius, as the name implies, is anomaly in which the heart is absent. Acardius can only occur in multiple gestations since its circulation must be maintained by vascular anastomosis with an accompanying fetus (2). Although little doubt exists that intrauterine growth of the acardiac twin is achieved by the perfusion afforded from the normal co-twin via vessel anastomosis in the placenta, the pathogenesis of acardia has been disputed. Some authors (3-5) have presented evidence supporting the concept that the primary defect is one of cardiac embryogenesis (dysmorphogenesis) and that the vascular anastomosis between the vessels, although necessary for the intrauterine survival of the acardiac twin, is not responsible for the cardiac findings. Others (6-8) believe that the primary cause is an abnormal vascular communication between embryos leading to reversed flow of blood to the hemodynamically
Acardiac anomaly: current issues in prenatal assessment and treatment

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Acardiac anomaly is a rare condition affecting monochorionic multiple pregnancies. We review this condition with emphasis on its prenatal diagnostic features and treatment options. Due to the parasitic hemodynamic dependence of the acardiac twin on the pump twin, it is important to monitor the pump twin for signs of decompensation and, if indicated, intervene by interrupting vascular supply to the acardiac twin. The goal of treatment is to maximize the pump-twin’s chance of survival. To assist with the decision of when to treat, we suggest a new classification system based on prognostic factors, specifically the size and growth of the acardiac twin and the cardiovascular condition of the pump twin. When the acardiac twin is small and no signs of cardiovascular impairment in the pump twin are present, we suggest serial ultrasound surveillance to detect any worsening of the condition. In cases with a large acardiac twin or rapid growth of the acardiac mass, we recommend prompt intervention. Once treatment is indicated, the intrafetal approach to interrupt the vascular supply to the acardiac twin appears to be superior to cord occlusion techniques as it is simpler, safer and more effective. The first line of treatment, if available, should be ultrasound-guided laser coagulation or radiofrequency ablation of the intrafetal vessels.

INTRODUCTION

Acardiac anomaly, one of the most severe human malformations, is a rare complication unique to monochorionic multiple pregnancies. In this condition, the primary malformation is the lack of a well-defined cardiac structure in one twin (the acardiac twin), which is kept alive by its structurally normal co-twin (the pump twin) through a superficial artery-to-artery placental anastomosis. Arterial blood flows in a retrograde fashion from the pump twin toward, rather than away from, the affected twin, which is why acardiac anomaly is also referred to as the twin reversed arterial perfusion (TRAP) sequence (Van Allen et al., 1983). The acardiac twin thereby acts as a parasite that is hemodynamically dependent upon the pump twin and, therefore, its continuous growth threatens the survival of the pump twin by stealing blood as well as acting as a space-occupying mass. Based on two large series reporting on the natural history of the condition, perinatal mortality rates of the co-twin range from 35 to 55% (Moore et al., 1990; Healey, 1994). Of note, no study has addressed the issue of short- and long-term morbidity of the surviving pump twins.

Acardiac anomaly occurs in approximately 1 in 35 000 pregnancies and in 1% of monochorionic twins (James, 1977; Napolitani and Schreiber, 1960). It has also been described in triplet, quadruplet and quintuplet pregnancies (Napolitani and Schreiber, 1960; James, 1977; Benirschke and Kaufmann, 1995). Due to misdiagnosis (Seckin et al., 2003) or significant shrinkage of the acardiac twin by the time of delivery, it is likely that many cases go unnoticed and the incidence of this condition may be, in fact, higher. According to one pathological series of 30 cases, one-third have a monochorionic-monoamniotic placenta and two-thirds are associated with a monochorionic-di amniotic placenta (Benirschke and Kaufmann, 1995).

In the past two decades, concurrent with technological advancements in diagnostic and therapeutic capabilities in the field of obstetrics, numerous reports have been published to describe acardiac anomaly in different clinical settings, possible prognostic factors that may influence its management, and techniques and outcomes of various modes of treatment. The aim of this article is to review the current knowledge of the condition, focusing on its prenatal assessment, management options and available invasive treatments.

PATHOLOGY

As a rule, the development of all organ systems is affected in acardiac anomaly. Consequently, the structure of the acardiac fetus is extremely variable. Some acardiac twins possess well-differentiated organ structures, while others lack any recognizable anatomy (Figure 1). Size can vary from small teratoma-like masses to fetuses more than double the size of its co-twin (Sato et al., 1983). The heart may be completely absent (holoacardia) or be in a primitive state of development (pseudoacardia). Most commonly, acardiac twins are accephalic with absent upper extremities. A central trunk is usually present with a well-developed or rudimentary
spine. Structures that are frequently absent include the heart (less than 20% of fetuses have identifiable cardiac tissue), head, upper limbs, pancreas, lungs, liver and small intestines. A two-vessel cord is found in more than two-thirds of cases (Healey, 1994). Due to the lack of communication between the lymphatic and vascular systems, the acardiac twin frequently develops severe subcutaneous edema and cystic hygromas, which can significantly increase the size of the fetus and distort the already abnormal anatomy.

The placenta in pregnancies complicated by acardiac anomaly has not been studied in great detail. However, all placentas have a similar pattern consisting of the presence of two anastomoses, one artery-to-artery and one vein-to-vein, connecting the circulation between the acardiac and the pump twins. In most cases, these anastomoses are on the placental surface and allow flow between the acardiac twin’s umbilical cord and the major arterial and venous branches of the cord of the pump twin. Occasionally, the cord of the acardiac twin inserts into the cord of the pump twin, in which case the umbilical arteries and veins of the twins are directly anastomosed and covered by Wharton’s jelly (Figure 2). As a result of this vascular connection, acardiac twins always lack functional placental tissue.

**PATHOPHYSIOLOGY**

The etiology and pathophysiology underlying acardiac anomaly are not completely understood. The two main theories attempting to explain the origin of acardiac anomaly are:

1. Abnormal placental vasculature leading to circulatory reversal with subsequent alteration in cardiac development;
2. Abnormal cardiac embryogenesis occurring as a primary event.

A major contribution to the knowledge of this complex anomaly was made by Van Allen et al. (1983), who first developed the TRAP sequence hypothesis. According to this theory, which is now accepted as an accurate description of the pathophysiology, arterial blood flows in a retrograde nature in the acardiac twin’s umbilical artery via a single artery-to-artery anastomosis. Consequently, poorly oxygenated and nutrient-poor blood bypasses the placenta, enters the circulation of the acardiac twin and passively follows a course through the iliac arteries at subnormal pulse pressures to preferentially perfuse the caudal rather than the cephalad structures. The blood flow then returns to the pump-twin’s circulation via a single vein-to-vein anastomosis. This circulatory event explains why the lower limbs of an acardiac twin are better formed than its more cephalad structures, as the latter receives more severely deoxygenated blood, resulting in abnormal development and atrophy of the heart and dependent organs. However, the TRAP sequence only describes the final stage of the process that results in continuous perfusion and growth of an acardiac fetus, failing to explain the mechanism leading to the persistence of the single artery-to-artery anastomosis and lack of placentation. In addition, this theory neither explains the development of a pseudoacardiac twin nor why some acardiac twins have a three-vessel cord.

Alternative etiologic theories have postulated that the primary event is a disturbance in cardiac embryogenesis that secondarily causes retrograde flow in the affected twin (Severn and Holyoke, 1973), for instance, due to chromosome abnormality (Benirschke and Kaufmann, 1995) or environmental factors (Wilson, 1972). Cytogenetic analyses have failed to demonstrate any consistent