Conservative management in a case of uncomplicated trap sequence: a case report and brief literature review

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Abstract

Introduction: twin reversed arterial perfusion (TRAP) sequence is a rare anomaly that occurs in monochorionic twins with overall mortality rate ranging from 50% to 70% in the normal fetus, above all for congestive cardiac failure.

Case report: a 31-year-old Caucasian gravida was referred to our fetomaternal medicine unit in the 25 gestational age. Ultrasound examination revealed a monochorionic, diamniotic twin pregnancy with a donor fetus showing normal morphology and growth corresponding to gestational age. The recipient twin appeared grossly abnormal with no head, upper limbs, heart, or thoracic structures and massive, diffuse, soft tissue edema. Fetal Doppler and fetal echocardiography revealed normal parameters. The patient refused any treatment and was monitored with weekly ultrasonography and Doppler ultrasound examination. She underwent cesarean section due to premature labor/rupture of membranes secondary to a mild polyhydramnios, at 36 weeks gestational age and delivered an apparent normal female live baby weighing 2550 gr, and another female *acardius acephalus* twin, birth weight 1300 gr. This baby had rudimentary edematous lower limbs, pelvic bone, lower sacral vertebrae, and absence of thorax and cephalic structures.

Conclusion: although the literature suggest that early intrafetal laser treatment of TRAP sequence is advantageous, our case shows that pregnancies referred late would still require a tailored approach after a risk-benefit assessment.

Key words: *acardiac twin, monochorionic, twin pregnancy, pregnancy complication, fetal malformation.*

Introduction

Twin pregnancy is relatively common, occurring in about 2- 3% of pregnancies, and they almost doubled over the last two decades as result of both increasing average maternal age and the use of assisted conception technologies (1).

In addition to abnormalities that also occur in singletons, there are specific anomalies unique to multiple pregnancies related to the underlying twinning process and aspects of placentation. Multiple pregnancies may be monozygotic (so-called 'identical') or polyzygotic ('non-identical' or 'fraternal'). The majority (about 70%) is polyzygotic, each embryo derived from a different ovum (2).

The pattern of placentation in monozygotic twins depends primarily upon the timing of the underlying twinning process, such that early division, within the first three days post fertilization, results in dichorionic placentation; twinning at approximately three to nine days post fertilization results in monochorionic twin placentation, and splitting after around nine days post fertilization results in monoamniotic twins (3).

Monochorionic (MC) twin pregnancies demonstrate varying degrees of unequal placental share, and almost all have inter-twin placental vascular anastomoses resulting in communication between the two fetoplacental circulations. All complications of MC twins are based on inter-twin discordance, encompassing fetal size, amniotic fluid volume, fetoplacental hemodynamics as well as structural defects.

Imbalance in the net flow of blood leads to development of twin-twin transfusion syndrome (TTTS) or twin reversed arterial perfusion sequence (TRAP), the most severe and specific complications in MC twin pregnancies. It is also known as *acardius chorioangiopagus parasiticus* and it is characterized by vascular anastomosis and partial or complete lack of cardiac development in one twin. This condition occurs in 1 in 35,000-40,000 pregnancies, representing around 1% of monochorionic twins (4, 5).

Pathophysiologically, there is lack of a well-formed cardiac structure in one fetus (acardiac) that acts as a parasite because it is haemodynamically dependent on the structurally normal co-twin (pump twin) through a superficial artery-to-artery placental anastomosis (2).

Without prompt detection, follow-up, and treatment, mortality rates for pump twins have been noted to be as high as 50 to 70% (6, 7).

We report a case of a primigravida, who came for routine antenatal checkup to our hospital at 25 weeks gestational age. Ultrasound imaging revealed twin monochorionic intrauterine pregnancy with a viable, normal-appearing first twin and amorphous structured second twin connected by umbilical vessels. She refused the treatment and decided to carry on the pregnancy, with an apparent normal live baby and an acardius acephalus fetus.

Case report

A 31-year-old gravida 1, para 0, Caucasian woman was referred to our fetomaternal medicine unit in the 25 gestational age, due to suspected anomalies of one twin without further specification. Ultrasound examination revealed a monochorionic, diamniotic twin pregnancy with a viable fetus showing normal morphology and growth corresponding to gestational age. Fetal Doppler and fetal echocardiography revealed normal parameters without any signs of cardiac failure (*donor*).

The second twin (*recipient*) appeared grossly abnormal with hydropic features and no cardiac activity. This fetus had an incompletely formed skeleton, with no head, upper limbs, heart, or thoracic structures (Fig. 1). It had an abdominal stump, with a cystic structure, possibly the urinary bladder, two abnormal lower limbs which showed massive, diffuse, soft tissue edema (Fig. 2).

On pulsed Doppler imaging, a single umbilical artery in the abnormal fetus was detected with reversal of flow on the spectral graph (Fig. 3). Ultrasound findings were consistent with TRAP sequence twin with an acardius acephalus.

The amniotic fluid was normal in both sacs and monochorionic placenta located in the anterior region. Complications and options treatment were discussed

Figure 2. The acardiac twin had an abdominal stump, with a cystic structure, possibly the urinary bladder, two abnormal lower limbs which showed massive, diffuse, soft tissue edema.

with the patient, but she opted to continue the pregnancy without any treatment.

The patient was monitored with weekly ultrasonography and Doppler ultrasound examination to assess the well-being of the pump twin and she didn't demonstrate any evidence of complications like cardiac failure, hydrops, and polyhydramnios during the follow-up. She underwent cesarean section due to premature labor/rupture of membranes secondary to a mild polyhydramnios, at 36 weeks gestational age and delivered an apparent normal female live baby weighing 2550 gr, and another female acardius acephalus twin, birth weight 1300 gr (Fig. 4). This baby had rudimental edematous

Figure 1. The acardiac twin had an incompletely formed skeleton, with no head, upper limbs, heart, or thoracic structures.

Figure 3. In the abnormal fetus, a single umbilical artery was detected with reversed of flow on the spectral graph on pulsed Doppler imaging.

Figure 5. The acardiac twin had rudimental edematous lower limbs, pelvic bone, lower sacral vertebrae, and absence of thorax and cephalic structures.

Figure 4. The delivered acardius acephalus twin was female weighting 1300 gr.

Figure 6. The single placenta showed direct anastomosis between the umbilical cords, a velamentous cord insertion and two vessel cord of the acardiac twin.

lower limbs, pelvic bone, lower sacral vertebrae, and absence of thorax and cephalic structures (Fig. 5).

The single placenta showed direct anastomosis between the umbilical cords, a velamentous cord insertion and two vessel cord of the acardiac twin (Fig. 6). The donor twin survived without detectable mid- or long-term sequelae such as revealed until the 4th year pediatric follow-up.

Discussion

Twin reversed arterial perfusion (TRAP) is a complication unique to monochorionic twins in which there is lack of a well-formed cardiac structure in one fetus (acardiac), abnormally perfused by a structurally nor-

mal co-twin (pump twin) through a superficial artery-to-artery placental anastomosis. Although the first case was described by Benedetti in 1533, very few cases have been reported in the literature since then (8).

The etiology and exact patho-physiological mechanisms are not well understood and the pathogenesis is controversial.

Two main hypotheses have been proposed (9):

1. *Aberrant placental vasculature*, with *abnormal artery-to-artery placental anastomosis* in early embryogenesis causes malformation of the acardiac twin (10). Imbalance in the blood pressure can lead to de-oxygenated blood-transfer from the healthy fetus (donor) to the impaired twin via the umbilical cord. This poorly oxygenated blood may

maintain a certain growth of near-by located structures like the lower limbs or the intestines. In contrast, the blood-circuit in more distant areas like head, upper extremities, thorax is insufficient and their development often shows an arrest. So the receiving twin is gradually transformed into a parasite-like organism dependent on the blood supply from the donating twin (11).

2. A primary *defect in embryogenesis* in one twin leads first to failure of cardiac formation, followed by secondary development of anastomosis between umbilical vessels allowing survival of affected twin (12).

A range of structural anomalies have been reported in the acardiac twin, presumably due to the abnormal perfusion, from relatively normal body forms with well-differentiated organ structures through to apparent amorphous structures with no recognizable normal anatomy (13).

The heart may be completely absent (*holoacardius*), represented by a rudimentary cardiac structure (*pseudoacardius*) or less than 20% have identifiable cardiac tissue.

The antenatal diagnosis of TRAP-sequence during ultrasound is feasible and can be readily established during the first-trimester-screening (14).

An acardiac twin may be detected sonographically by showing fetal movement and growth, without definite differentiation of head and trunk. Commonly maldeveloped upper and lower extremities, without an evident heartbeat can be seen (15). The acardiac twin frequently has severe subcutaneous oedema and cystic hygromas, which can significantly, increase the size of the fetus (2).

Depending on the morphology of the acardiac fetus, four distinct types have been described in the literature (16):

1. *acardius acephalus*: is the most common type, 60-75% of cases, with well-developed pelvis and lower limbs, but no head, usually no thoracic organs and often no arms
2. *acardius anceps*: the most differentiated type of acardiac twins with well-developed body and extremities, but only a partially formed head and face; approximately 10% of cases
3. *acardius acormus*: in which only cephalic structures were detectable with a close umbilical cord insertion; this is very rare, about 5% of cases
4. *acardius amorphus*: in which the fetus is represented by a shapeless mass of tissue containing no recognizable structures; approximately 20% of cases.

Although this anatomical/pathological classification system has been widely used, it has no direct correlation with pregnancy outcome or implications for management, and it has been suggested that prenatal classification may be more appropriately based on the size of the acardiac twin and the apparent condition of the pump twin (16). Effectively the acardiac size may vary from incidental structures to large masses more than double the size of the pump twin, the largest re-

ported acardiac fetus weighing >6 kg (2).

The overall perinatal mortality of pump twins is 50-55% and appears to correlate with the size of the acardiac twin. A higher weight of the recipient twin, with multiple internal organs, is more likely associated with a significant increase in the cardiac output and therefore perinatal mortality of the pump twin, generally due to cardiac insufficiency (17).

This high cardiac output also increases perfusion of the fetal kidneys, resulting in overproduction of fetal urine and polyhydramnios, leading to premature delivery (before 32 weeks 'gestation) and prematurity (18).

The weight of the acardiac twin cannot be calculated using the standard formulae (such as Hadlock's), from the values of the head circumference, abdominal circumference, and femur length.

Instead, it is derived by the following formula: $(1.2 \times \text{longest length}^2) - (1.7 \times \text{longest length})$ (19).

Recently, Wong and Sepulveda suggested the role of *abdominal circumference ratio* as a prognostic factor in evaluating the impact of the acardiac fetus on the pump twin (17). When the ratio of the weight of the acardiac fetus to the weight of the donor fetus is greater than 70%, the incidence of preterm delivery is 90%, that of polyhydramnios is 40%, and that of congestive heart failure in the pump twin is 30%. In comparison, the corresponding rates are 75, 30, and 10%, respectively, when the ratio is less than 70% (17).

Doppler interrogation shows pathognomonic flow-pattern in terms of reversed arterial perfusion from the pumping twin towards the parasitic twin and in most of the cases (75%) reversed arterial blood supply enters the acardiac twin via a single umbilical artery. Venous blood-flow shows reversed perfusion as well (20, 21).

Over the last two decades several procedures have been introduced aimed at establishing a permanent separation of the two blood-circuits of the twins improving prognosis and mortality in the pump fetus.

These techniques partly target the umbilical cord vessels using coil occlusion ligation, laser coagulation or bipolar coagulation. Other methods are aimed at the intrafetal umbilical vessels using alcohol injection, thermocoagulation, laser coagulation, radiofrequency or, very recently, high-intensity focused ultrasound (22). Laser coagulation of the vascular anastomoses on the placental surface has been proven as an effective and safe measure in many studies and case reports (23). Ultrasound-guided intrafetal needle approaches are easier and less invasive.

Nevertheless there is ongoing discussion regarding the correct management, expectant or not, and the exact intervention timing. TRAP sequence can be treated in 3 different ways, depending on the condition of the pumping twin (24):

- tailored approach with expectant management, until sonographic evidence of compromise in the pump twin (25) (polyhydramnios with a vertical pocket above 8 cm, cardiac dysfunction, abnormal Doppler-flow-patterns and/or hydrops); this expectant management has the advantage of

- avoiding an intervention that itself can cause miscarriage
- prophylactic intervention at 16-18 weeks after obliteration of the celomic cavity to reduce the risk of miscarriage (26)
 - prophylactic intervention at 12 weeks to avoid the risk of death of the pump twin between 12 and 16 weeks (24).

However the presence of relatively large weight acardiac twin, or monoamniotic twins are two parameters mandatory for early intervention (23).

Conservative management includes different tocolytic approaches and digitalis-treatment to support the cardiac performance of the pump twin (27). Regular sonographic evaluation of high-risk markers, including the amniotic fluid index of the pumping twin is recommended.

Amniotic drainages, or indomethacin-treatment may be performed to reduce the amniotic volume and to avoid premature labor, without notable side-effects (27), and improve prognosis in the survival fetus through reduction of the amount of amniotic fluid. The outcome of conservative management when acardius weight is < 50% of that of the pump twin, has been reported to be favorable in 88% of cases (28).

Some Authors, however, reported high pregnancy loss rates with the expectant management, even in cases of spontaneous cessation of flow in the acardiac twin. Lewi et al. (24) demonstrated that 11 (84.6%) of 13 of a cohort of pump twins with TRAP sequence diagnosed in the first trimester had a fatal outcome after expectant management. Other Authors reported loss rates, following diagnoses in the first trimester, of 83-100% with all losses occurring at $\leq$ 16 weeks (26, 29).

The constantly increasing number of first-trimester diagnoses, together with the high loss rates reported in the pump twin if expectant management is chosen until 16 weeks, has raised the interest in earlier intervention in the first trimester and the recent studies add some evidence in favor of prophylactic intervention by intrafetal laser from 12 weeks onward.

Recently Berg et al. have registered in their experience fetal-loss rate from the first trimester onward was lower than previously reported. Expectant management in cases diagnosed at $\leq$ 14 weeks was associated with a fetal loss rate of 42.9%. After spontaneous cessation of flow to the TRAP twin, only 20.0% of pregnancies ended with death of the pump twin and there was no evidence of brain damage at the follow-up scans in the neonatal period (21).

In our cases, the patient refused any operative procedures, and an unique expectant management was adopted with weekly B-mode, and Color-Doppler examination. All the pregnancy duration was made without any sign of complication in the pump twin and the deliver occurred about at term. What exactly causes progressive decompensation of a pump twin is unknown. Similar cases, treated with conservative management and without any developed complications, however, suggest a certain amount of resources to

keep the blood-circuit of the pumping twin successfully working for quite a long time.

Conclusion

TRAP sequence is an extremely rare congenital anomaly, of which antenatal diagnosis is feasible and can be established during the first-trimester screening. The obstetrician should be aware of this anomaly especially in twin/multiple pregnancies so that timely proper measures can be taken to survive the pump twin, according to gestational age at the time of diagnosis.

Though many patients can benefit from conservative treatment, recent trend toward using minimally invasive treatment modalities for the vascular anastomosis has been a benefit in improving the outcome of the pump twin when the diagnosis is established at an early age.

The correct and appropriate management isn't yet established and there are no ultrasound signs in the first trimester that can help to distinguish between the pump twin at risk of death from those that will survive. Much larger studies are necessary to examine whether prophylactic intervention at 12 weeks is more advantageous preventing the death of those who would have died before 16 weeks without worsening the survival of those who are currently treated at 16 weeks.

Although the literature suggest that early intrafetal laser treatment of TRAP sequence is advantageous, our case shows that pregnancies referred late would still require a tailored approach after a risk-benefit assessment.

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