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A Case Report on Twin Reversal Arterial Perfusion Sequence in a Resource Poor Setting - Diagnostic and Management Challenges

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1. Abstract

Twin reversal arterial perfusion sequence is rare, and the most extreme complication of monochorionic monozygotic multiple gestation. Characteristically, there exists a recipient "acardiac" fetus that depends on the other donor, "Pump" fetus. The donor twin-pump fetus often appears grossly normal, and supplies the recipient twin with poorly oxygenated blood through the placental arterio-arterial anastomosis. The resultant effect in the recipient "acardiac' fetus is abnormal differentiation and development of organs with a mortality rate as high as 100%. Treatment is aimed at enhancing the pump twin survival. In resource poor countries, diagnosis and management can be challenging due to poor uptake and availability of tools and/or skills. This is a case report of an unbooked 32-year-old multipara who presented at an estimated gestational age of 27 weeks and 5 days from a private facility with an obstetric ultrasound scan finding of death of the second twin. She was managed conservatively until the gestational age of 30 weeks and 4 days when she had a caesarean section due to worsening maternal respiratory distress. She was delivered of a set of twins; twin 1- a live male neonate with excess liquor and twin 2- oedematous dead fetus with multiple anomalies. we describe a case of an incidental finding of a dead fetus with multiple anomalies suspected to be an acardiac twin. TRAPs are a rare complication of monozygotic gestation. High index of suspicion and detailed evaluation with an obstetric Doppler ultrasound scan for antenatal surveillance in multiple gestations, especially monozygotic is highly recommended.

2. Introduction

Multiple gestation is a high-risk pregnancy associated with obstetric complications and fetal congenital anomaly. When compared to singleton gestation, multiple gestation is twice the risk of fetal anomaly [1]. Some of these complications include preterm contraction, preterm labour/delivery, dysfunctional labor, risk of operative abdominal/vaginal delivery, gestational hypertension, anaemia in pregnancy, obstetrics hemorrhage among others, while structural anomalies include discordance twin, twin-to-twin transfusion syndrome, twin reversal arterial perfusion syndrome [1-4]. Twin reversal arterial perfusion sequence [TRAPs], also known as acardiac twin, is uncommon, but it is the most extreme complication of multi-fetal pregnancy. It occurs exclusively in monochorionic monozygotic gestations [1]. Characteristically, there exists a recipient twin with variable lethal anomaly and a grossly normal pump twin, though few cases of isolated congenital anomaly in the pump twins have been recorded [2]. The incidence of TRAPs is about 1% among monozygotic twins, and 1 in 35000 of all deliveries [3]. A recent study reported a higher incidence, which was attributed to increasing incidence of artificial reproductive techniques and increased uptake of first trimester ultrasound evaluation as a diagnostic tool. In monochorionic twins, Van Gemert et al reported an incidence of almost 3%, which equates to about 1 in 9500-11000 pregnancies [4]. The exact aetiology and risk factors remain unknown. In the pathophysiology of TRAPs, there is a reversal of blood flow through the anastomosis of both umbilical arteries as the donor twin pumps blood to the recipient [5]. This

results from the absence of a heart that works in the acardiac twin. The recipient twin is supplied with blood lacking enough oxygen, which then goes to the lower extremities. This inadvertently worsens the oxygen lack in the blood circulating other parts of the fetus. The relative tissue and organ hypoxia in the cranial part result in different grades of impaired growth and differentiation of the organs in the cranial portion [5]. While the recipient twin has a mortality rate as high as 100%, the pump twin is at risk of high output failure, preterm labour and birth from polyhydramnios, and poor perinatal outcome. The reported risk of mortality varies between 35-50% [6].

3. Case Report

Mrs. S.F is an unbooked 32-year-old Gravida 6 Para 4+1[4Alive]. She is a house wife with primary education who presented at a gestational age of 27 weeks and 5 days from a private facility with incidental finding of death of second twin on obstetric ultrasound scan. She presented for booking of the pregnancy at the source of referral, where she had an obstetrics ultrasound scan that revealed the above findings. This necessitated referral to UCH. She had no complaints at presentation, and there was no history of chronic medical illness. The index pregnancy was conceived spontaneously. The physical examination at presentation revealed a conscious woman, not pale and acyanosed. The vital signs were within normal limits. The abdomen was uniformly enlarged and moved with respiration, the symphysio-fundal height was 34cm and fetal parts were difficult to palpate. The fetal heart tone for twin 1 was audible. A repeat obstetrics scan done demonstrated intrauterine twin gestation, with the first twin in longitudinal lie, cephalic presentation at gestational age of 28 weeks, with estimated fetal weight of 1.26kg and deepest vertical pool [DVP] of 15.8cm. The umbilical artery Doppler parameters for twin 1 were normal. A second twin in transverse lie, both cardiac activity and gross body movements were absent. The DVP was 14cm, and estimated fetal weight was 356g at an estimated gestation age 19 weeks. She was counselled on diagnosis, implication, complications, she was managed conservatively. She had antenatal corticosteroids; intramuscular dexamethasone 6mg 12 hourly for 48 hours. The full blood count parameters were within the normal range, and blood type was “O” Rhesus positive. The weekly coagulation profile was normal. Serial obstetrics Doppler ultrasound scan showed worsening levels of polyhydramnios. Though, the umbilical Doppler indices of the viable twin remained normal. At gestational age of 30 weeks and 4 days, she developed respiratory difficulties due to marked abdominal distention, and she subsequently had abdominal delivery due to worsening respiratory symptoms. The intraoperative findings were: twin gestation with monochorionic-diamniotic placentation. The leading twin was a live male neonate, delivered in a pool of clear, copious liquor in excess of 2.2L, the birth weight was 1.2kg, and APGAR was 6 at 1st and 8 at 5th minute. The second twin was a lifeless severely malformed male neonate, with generalized edema, the head and thoracic region were grossly deformed. There were rudimentary facial structures suspected to be the eyes, nostrils and mouth. The fetus was grossly edematous. The birth weight was 3.0kg (Figures 1-2). The first twin was admitted into the Neonatal Care Unit on account of prematurity, but died on 4th day of life from respiratory distress syndrome. The postoperative management of the mother was uneventful, postoperative vital signs and packed cell volume were normal; and she was subsequently discharged to the post-natal clinic. At the post-natal clinic at 6 weeks, she had no complaint and the clinical condition was good.

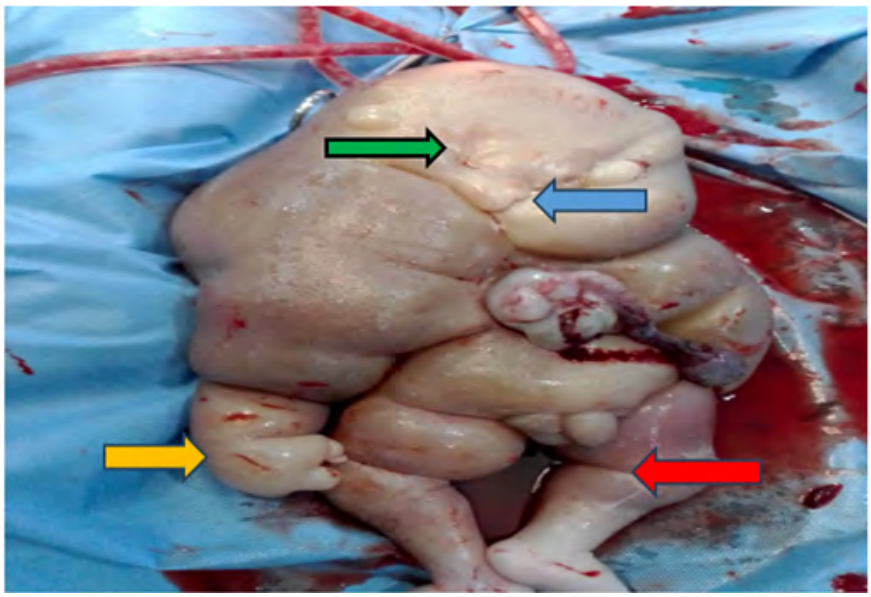

Figure 1: Front view of the acardiac baby, with deformed thoracic, upper limbs and cranial region. The cranial part shows rudimentary buds to suggest facial structures. Green arrow – Eyes, Blue arrow – nose, Yellow arrow – upper limb, and red arrow – lower limb.

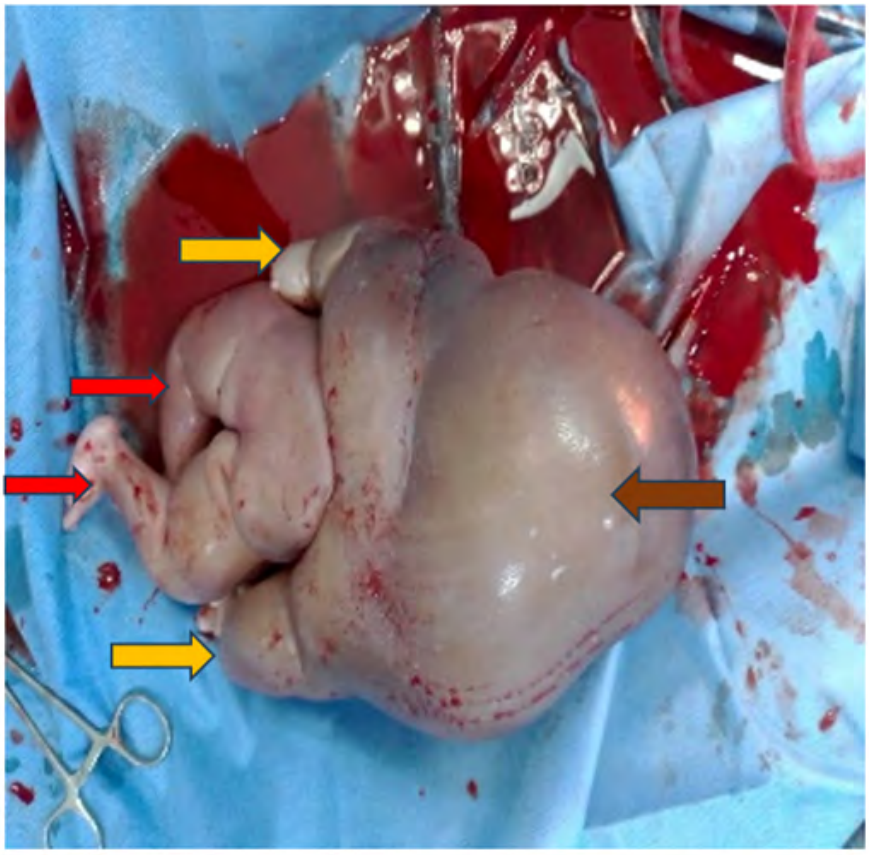

Figure 2: Posterior view of the acardiac baby. Brown arrow – Head, Blue arrow – nose, Yellow arrow – upper limb, and Red arrow – lower limb.

4. Discussion

This is a case report of an incidental finding of a Twin Reversed Arterial Perfusion Sequence [TRAPs] at delivery of a woman with multiple gestation and demise of one twin. The patient presented with an unsuspected finding of intrauterine gestation with live first twin and demise of second twin on routine obstetric ultrasound scan. Fetal congenital anomaly or TRAPs malformation was not detected in earlier ultrasound scans. TRAPS is an uncommon complication of monochorionic monozygotic twinning. In the 1500s, Benedetti documented the first ever recorded cases of TRAPS, and many more cases have been reported. [7] In 1978, Lehr and Dire reported the first antenatal diagnosis of an acardiac twin [8]. The embryogenesis is due to the absence of anatomical and physiologic heart in the recipient fetus [also known as the acardiac twin], and an arterial anastomosis within the placental circulation through which the acardiac fetus is perfused by the donor twin. This is demonstrable in the prenatal period, with evidence of blood flow reversal in the umbilical artery of the recipient twin on obstetric Doppler ultrasound. TRAPS affects about 0.3-1% [7, 9] of monozygotic gestations, and has an approximate incidence of 1 in 35,000 births. [10, 11]. Rarely, it may occur with higher-order multifetal pregnancies [12]. The aetiology remains poorly understood; thus, it is reported to occur indiscriminately. A disrupted embryogenesis has been postulated to incite abnormal growth in the recipient fetuses, a vascular anastomosis, and the vascular support dependence of the acardiac fetus on the predominant pump fetus [13, 14]. TRAPS results from an unusual anastomosis between placental arteries [15]. Classically, this results in one viable twin, which acts as the pump fetus, with a 9% risk of chromosomal abnormalities, and one non-viable twin [recipient/acardiac twin]. Characteristically, four morphological types, namely; acephalus, anceps, acormus and amorphous, have been described. The circulation in the lower extremities through the iliac arteries is prioritized when the recipient fetus is supplied with deoxygenated blood by the donor twin, leading to atrophy of the heart and brain, a consequence of poor perfusion. Ultimately, peculiar anomalous features develop. The acardiac twin may be associated with single umbilical artery and chromosomal anomaly in 66% and 33% cases respectively [16]. The non-viable fetus increases the risk of perinatal death of the viable pump twin up to 55% [17] by three main mechanisms. Firstly, the rise in cardiac activity has the propensity to cause congestive heart failure and polyhydramnios of the pump twin. Secondly, the uterine over-distention and associated polyhydramnios may result in preterm premature rupture of membranes [pPROM], preterm labor and delivery; and lastly, a small for gestational age donor twin with hypoxic tissues and organs, a sequela of reversal of flow of blood with reduced oxygen concentrations to the donor fetus via the arterial anastomosis. In this case report, the woman had preterm delivery due to the uterine over-distention from polyhydramnios, which ultimately resulted in the splitting of the diaphragm and respiratory distress reported. Vitucci et.al. reported factors that could predict poor prognosis of the pump twin, these

include [18]; presence of biventricular heart failure manifested as hydrops or polyhydramnios, preterm delivery <32 weeks, a huge acardius described as an "acardiac-to-pump twin weight ratio>70%", inconsistencies in the pump/acardiac umbilical venous diameter [UVD] ratio, and the occurrence of a well-formed upper body and extremities in the acardiac twin. The pump/acardiac UVD ratio gives the extent of the excess pump cardiac output [19] and Van et.al, 2016 found this parameter as the most reliable predictor of fetal outcome [20]. A study done by Tan et al, reported that the acardiac-to-donor twin weight ratio ≥ 0.7 correlates with significant complications of polyhydramnios, preterm delivery, congestive heart failure [21]. The acardiac to pump twin weight ratio in this case was 2.5. The high acardiac to donor twin weight ratio, delivery before 32 weeks, and presence of hydrops and polyhydramnios in the case reported could explain the poor prognosis of the donor twin. Ultrasound is the main diagnostic tool. An acardiac twin should be considered when a morphologically abnormal fetus is detected in a monochorionic twin pregnancy [11]. Other notable ultrasonographic findings are marked discrepancies in fetal biometrical measurements, commonly the abdominal girth; absence of an anatomically and functionally normal heart in one twin associated with variable forms of abnormalities involving the cranial part, torso and limbs; presence of hydrops in the diseased twin. In few cases, an arrhythmia may be found due to the presence of an embryonic heart beat or the pulsation from the flow reversal. A unique finding in the first few weeks of pregnancy is the colour Doppler ultrasound demonstration of reversed blood flow in the acardiac twin, with arterial circulation moving in the opposite direction, as well as in the abdominal aorta. [7] The death of a malformed monochorionic twin could mimic an acardiac fetus, but continued development at successive scans gives the accurate assessment. In these cases, ultrasound evaluation of the fetus suspected of intrauterine death should elucidate the lack of circulation. The diagnosis of TRAP sequence should be considered in the presence of persistent fetal circulation. Rare differentials, such as Intra-amniotic or placental tumors are possibilities, but the discovery of the skeleton or the umbilical cord attachment is suggestive of TRAPs [7]. Management is aimed at improving the clinical outcome of the donor fetus and ensuring that the pregnancy reaches term. The morphologic classification is of no importance in management and prognosis. Wang et.al proposed a classification of importance in management and prognosis [17]. Wang classified acardiac twin into type 1 and II. Type I is described as a "small or medium-sized acardiac twin, with an abdominal circumference ratio ≤50%" and type II as a "large-sized acardiac twin with an abdominal circumference ratio ≥ 50%". Each can be further sub-classified into "a" or "b" depending on absence or presence of features of heart failure in the viable twin. Prognosis is reassuring for the pump fetus in Type Ia acardius twin, which provides the opportunity to manage the pregnancy conservatively through scheduled fetal surveillance using the multidimensional fetal assessment. In more than 80% of cases, these babies do well with favourable prognosis. [22] When dealing with acardius TypeIb, it is imperative to monitor through serial ultrasound scans for an improvement or an unfavourable status that may warrant a non-conservative approach. The detection of a big fetus in acardius Type IIa may be attributed to hydrops and in some other cases, subcutaneous edema. Both have the propensity to predispose to preterm delivery, hence, intervention must be commenced as early as possible. When Type IIb acardius is discovered, immediate treatment must be instituted. Treatment was initially targeted at relieving maternal and fetal complications. For instance, inotropes like digoxin was used to prevent cardiac failure in the donor twin, prostaglandin synthase inhibitors was used to reduce polyhydramnios and risk of preterm labour. Serial amnioreduction was also employed too, as temporary control measures of polyhydramnios. The understanding of the pathologic basis has led to causal therapy directed at stopping the abnormal blood flow patterns between the twins. Since the first invasive therapy to deliver the acardiac twin at an earlier gestation and pump twin at a much later gestation by Robie et al in 1989, advances in therapy directed at fetal cord occlusion and intra-fetal vessels ablation has emerged. Cord occlusion can be achieved via various techniques including: endovascular cord embolization; [23] occlusion with laparoscopic guidance; [23, 24] hysterotomic incision, handling, exposing and occluding the umbilical cord through ultrasound guidance; [25] artificial thrombogenesis by employing the use of suture material saturated with alcohol,[26] fibrin, dextrose and surgical tissue adhesives like butyl cyanoacrylate.[21] The intra-fetal approach in contrary, has the ability to occlude the pelvic arteries and aorta of the recipient twin. Though, both cord occlusion and intra-fetal ablation techniques have been used by several clinicians, Tan et al reported better outcomes in terms of a much-reduced rate of failure [13% vs 35%, p= 0.03], a reduced occurrence of preterm delivery or rupture of membranes [23% vs 58%, p= 0.003] and an improved efficacy [77% vs 50%, p= 0.02] when invasive ablative techniques were employed. [21]. The best gestational age for the invasive intervention is controversial, though most studies reported higher rates of pump-fetus loss when performed in the first trimester [28, 29] Villie et al reported 4 cases of TRAPs treated by endoscopic cord coagulation at 17 weeks, 20 weeks, 26 weeks and 28 weeks respectively. Cases treated at 17 and 20 weeks showed successful arrest of circulation to the acardius twin and delivery of a healthy pump twin after spontaneous onset of labour at 29 weeks. On the contrary, the same intervention failed in the cases treated at 26 and 28 weeks. This was attributed to the edematous umbilical cord. Therefore, it was recommended that other treatment modalities should be employed at latter gestation, while in mid gestation, cord occlusion is associated with optimal outcome.[30] Recently, Aldiansyha et al. reported the first successful endoscopic bipolar cord

coagulation and amniopatch in Indonesia at 26 weeks gestational age [31].

In this case report, the diagnosis was missed during the prenatal period. The clinical features of severe polyhramnios evidenced by marked uterine over-distention with breathing difficulties, and a large deepest vertical pool [DVP > 8cm] of amniotic fluid on an obstetric scan, were noted. Polyhydramnios is a known complication, and a risk factor/precipitant of preterm labour/delivery associated with TRAPs. Poor health seeking behavior, late commencement of prenatal care, and poor access may be seen in women in resource poor settings, and more commonly multigravidae show poor health altitudes [32]. This is reflected in the case reported, as the first obstetrics scan was done at 27 week gestation. The first pregnancy ultrasound scan is recommended in the first trimester between 9-10 weeks. [33] The number of gestational sacs and chorionicity of multiple gestation is best determined by a first trimester sonographic evaluation [34, 35]. The delay in sonographic evaluation of the pregnancy and failure to establish the chorionicity precisely contributed to misdiagnosis from time of presentation. An obstetrics Doppler scan of the non-viable fetus would have given a clue to the diagnosis, but this was not done, as the attention was on the viable fetus. The diagnosis of acardiac fetus was made at delivery based on the physical appearance. The post-mortem evaluation was discussed and requested, but it was declined by parents. In resource poor setting, uptake and acceptance of post mortem evaluation is poor [36]. This would have been a viable alternative to establish the diagnosis. Furthermore, the established therapeutic interventions/techniques; cord occlusion and intra-fetal ablation, and required skills are not readily available, accessible and affordable in our setting.

5. Conclusion

Though TRAPS is a rare complication of multi-fetal gestation associated with significant perinatal mortality. There has been improvement in rate of survival of the “pump” fetus in the last few decades in developed settings, due to improvement in diagnostic skills/facility and therapeutic interventions. During routine obstetric ultrasound examination of multi-fetal gestation, findings of demise or morphologic abnormality of one fetus, should prompt careful Doppler assessment of all fetuses. Low- and middle-income countries need to invest in human and non-human resources and develop protocols for her Fetal & Maternal Medicine Units.

6. Patient Consent

Consent was obtained from the patient for the publication of this case.

7. Conflict of Interest

The authors have no conflict of interest to declare.

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