Gynecology & Obstetrics
ISSN: 2161-0932

Aitken et al., Gynecol Obstet (Sunnyvale) 2014, 4:9
DOI: 10.4172/2161-0932.1000239

Case Report Open Access

Early Radiofrequency Ablation for Twin Reversed Arterial Perfusion (TRAP) Sequence: Case Report and Literature Review

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Abstract

Background: High output cardiac failure resulting in fetal death or severe prematurity is a common complication of twin reversed arterial perfusion (TRAP) sequence. Various minimally invasive prenatal interventions have been proposed to improve outcomes for the pump fetus. Uncertainty still exists regarding the optimal timing of these interventions. Early intervention may protect the pump twin against prematurity from complications of cardiac failure or unexpected fetal death, although it carries a risk of procedure related pregnancy loss. Expectant management with surveillance and performing an intervention later in gestation if necessary' would potentially avoid some procedures but does not protect against unexpected fetal death.

Case: A healthy 30 year-old woman, gravida 2 para 1, was diagnosed with TRAP sequence at 13^{+1} weeks gestation. An uncomplicated ultrasound guided Radiofrequency Ablation (RFA) procedure ablating the vessels in the parasitic mass was performed at 15^{+0} weeks. The remainder of the pregnancy was uneventful and resulted in a term vaginal delivery of a healthy infant.

Conclusion: Based on our current knowledge of TRAP sequence and current instrumentation for fetal surgery, early occlusion of the vessels perfusing an acardiac fetus appears feasible and safe. Randomized trials on timing of intervention are urgently needed.

Keywords: Twin reversed arterial perfusion sequence; Monochorionic twins; Radiofrequency ablation; Timing; Fetal surgery

Introduction

Twin-Reversed Arterial Perfusion (TRAP) sequence complicates approximately 1% of monochorionic twin gestations and 1 in 34,600 deliveries [1,2]. Although its exact etiology is unknown, discordant development between two fetuses sharing a single placenta is essential for TRAP to occur. Intra-uterine fetal death, or a severe cardiac anomaly in one fetus leads to insufficient cardiac pump function to maintain its body perfusion. As a result of placental vascular anastomoses between the two fetal circulations, which are present in monochorionic twins, the healthy co-twin in some circumstances can maintain the perfusion of the demised fetus *in utero* [1]. This is visible on Doppler ultrasound as reversed umbilical arterial blood flow from the normal 'pump' twin to the acardiac tissue via an artero-arterial inter-twin anastomosis [3,4]. The acardiac mass is perfused with deoxygenated blood and the low oxygen content in the tissues results in grossly abnormal development and the hydropic appearance of the acardiac fetus. Doubly deoxygenated blood travels back from the acardiac twin to the pump twin through a veno-venous anastomosis [4] (Figure 1).

Sustained increased demands on the heart of the healthy pump fetus, which is perfusing two fetal 'bodies', may lead to high-output cardiac failure, especially when the acardiac fetus is large [5]. Heart failure can be visualized on ultrasound as atrial and ventricular enlargement, polyhydramnios and ultimately hydrops and fetal death. Severe heart failure occurs in 10-30% of cases, dependent on the size of the fetal mass. Polyhydramnios, and sometimes also the large volume of the acardiac mass often lead to preterm delivery, which occurs in 75-90% of cases [3,5-8].

The high risk of perinatal complications provides the indication for antenatal intervention: interruption of the blood flow from the pump twin to the acardiac mass. This is performed in order to terminate the non-viable acardiac fetus, thereby eliminating the risks of cardiac failure to the viable pump twin and reducing the risks of intrauterine death and preterm birth to the surviving fetus. Different modalities to interrupt the vascular flow to the acardiac fetus have been applied in clinical practice. The two most commonly used techniques are bipolar cord coagulation and, more recently, Radio-Frequency Ablation (RFA). The latter procedure has the advantage of a smaller entry port as it is a needle procedure and is technically straightforward. As outcomes appear similar with both methods [9], RFA has gained increasing popularity over the last 5 years [10,11].

RFA for acardiac twin pregnancy is associated with a 80% survival rate for the pump twin, with a mean gestational age at birth of 33.4 weeks [12]. These rates compare favourably with rates after no intervention or cord occlusion [13]. The risks of RFA include preterm premature rupture of membranes, preterm labor, loss of the pump twin from prematurity or intrauterine demise and thermal injury to the pump twin.

Despite the availability of intrauterine therapy, there remains some uncertainty in the management of TRAP. First, it is unclear whether therapy should be offered prophylactically to every patient diagnosed with TRAP or only to the 50-75% of cases in whom the acardiac mass becomes large resulting in high output cardiac failure in the pump twin or preterm labor. Secondly, there is uncertainty regarding optimal procedure timing: whether a prophylactic cord occlusion procedure should be offered after 16-18 weeks, after fusion of amnion and chorion, or earlier in pregnancy.

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Received June 19, 2014; **Accepted** August 31, 2014; **Published** September 05, 2014

Citation: Aitken K, Andrews J, Mieghem TV, Windrim R, Kachura J, et al. (2014) Early Radiofrequency Ablation for Twin Reversed Arterial Perfusion (TRAP) Sequence: Case Report and Literature Review. Gynecol Obstet (Sunnyvale) 4: 239 doi:10.4172/2161-0932.1000239

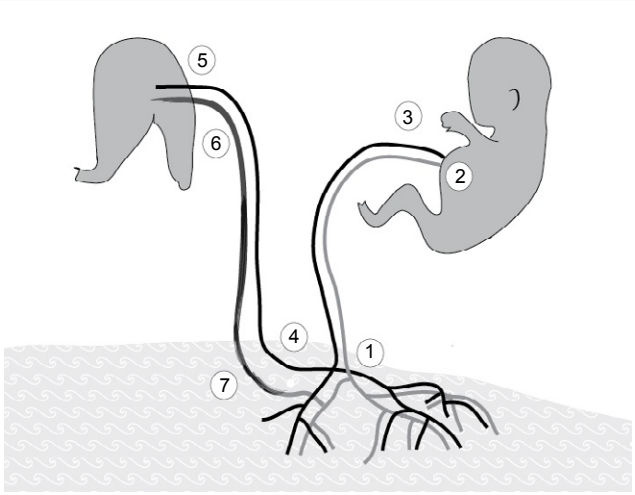

Figure 1: Circulation through the inter-twin anastomoses. Oxygenated blood travels from the placenta to the pump twin via the umbilical vein (1-2). Most of the deoxygenated blood is returned to the placenta from the pump twin via the umbilical artery (3-4), while some is diverted into the umbilical artery of the acardiac twin via an artero-arterial inter-twin anastomosis (4-5). Doubly deoxygenated blood then travels from the acardiac twin via the umbilical vein to the veno-venous anastomosis (6-7), infusing the oxygenated blood supply of the pump twin with doubly deoxygenated blood (7-1).

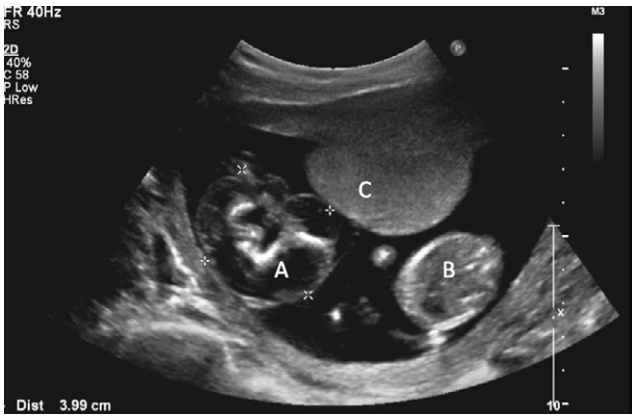

Figure 2: Ultrasound image pre-procedure. A: cross-section of upper pole of acardiac twin. B: cross-section through thorax of pump twin. C: placenta.

The case presented here raises these issues and provides the opportunity for discussion of the recent literature regarding the management of TRAP sequence. Informed consent for publication of the case was received from the patient.

Case

A 30 year-old woman, gravida 2 para 1, was diagnosed, and referred, with monochorionic diamniotic twins complicated by TRAP sequence at 13^{+1} gestation by last menstrual period (LMP) (12^{+6} by crown-rump length). After discussion with the referral Fetal Therapy centre, she made arrangements to travel to the referral centre for assessment and procedure at 14^{+5} weeks. The pump twin's size was estimated at 113 g, appropriate for dates, and its anatomy appeared normal. There was no evidence of hydrops. A clear membrane was seen separating both fetuses. The acardiac twin was comprised of a hemithorax, and abdomen, a small rudimentary upper extremity, and well-developed lower limbs, with no cardiac or cranial structures (acardiacus acephalus). The mass measured 40×41×52 mm and showed significant subcutaneous edema and cysts at the cephalad pole (Figure 2). Employing the prolate ellipse formula the product of the 3 dimensions multiplied by 0.523 yields a volume of 44.6 mL. Assuming a volume of 44.6 mL and tissue density similar to water (1 g/mL), the acardiac/pump twin ratio would be 39.4%. The amniotic fluid appeared normal around both fetuses. The placenta was located posteriorly. The pump fetus had a three-vessel cord. The acardiac's cord was short, contained only 2 vessels and inserted very close to the pump's cord on the placenta. The amnion and chorion were only partially fused.

At our institution management is decided on a case-by-case basis and options include pregnancy termination, expectant management or interruption of the vessels feeding the acardiac mass. After counseling, the patient decided to undergo RFA ablation of the acardiac vessels. This was performed at 15^{+0} weeks gestational age under local anesthesia with intravenous sedation with remifentanyl. A soloist 16.5G needle (Boston Scientific Corporation, 100 Boston Scientific Way Marlborough, MA 01752-1234 www.bostonscientific.com) was introduced in the right upper quadrant of the uterus in a region free of placenta and maternal vessels. The needle was then inserted into the acardiac fetus and advanced to the region between the bifurcation of the umbilical artery, vein, and descending aorta (Figure 3). In this position, two uncomplicated RFA coagulation episodes of four minutes each were completed. Following the procedure, absence of blood flow to the acardiac twin was confirmed with Doppler ultrasound.

Following a successful External-Cephalic Version (ECV), a healthy female infant was delivered vaginally at 40^{+2} weeks gestation. Birth weight was 3569g with Apgar scores of 10 at one minute and 10 at five minutes. The acardiac sac was visible at delivery as a translucent sac containing clear fluid and a small fetus measuring 3.4×2 cm in greatest dimension. This was compatible with all the post-procedure ultrasound measurements.

Discussion

We describe a case of early 'prophylactic' therapy for TRAP sequence in a monochorionic diamniotic twin pregnancy.

The natural history of TRAP has shown that an acardiac twin with an estimated fetal weight of ≤ 50% that of the pump twin (small-TRAP or sTRAP) is more likely to have a benign outcome. Hence conservative management has been proposed as a safe option in such cases. Conversely, an acardiac twin weighing >50% of the pump twin is associated with a high risk of preterm delivery and pump

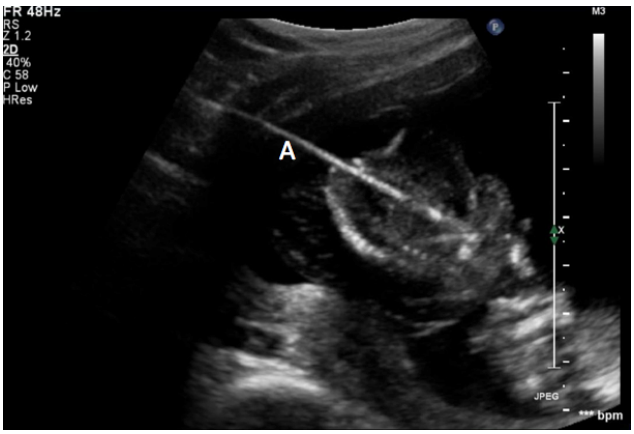

Figure 3: Ultrasound during procedure. A: RFA needle.

twin heart failure-related death. Therefore, the literature supports intrauterine intervention where the relative size of the acardiac twin is >50% that of the pump twin [1]. While complications may be predictable based on acardiac twin mass, growth of the acardiac twin is unpredictable, thereby complicating decisions surrounding therapy in the first and early second trimesters. It has been suggested, then, that following a diagnosis of TRAP sequence, weekly ultrasound should be performed to monitor for decompensation of the pump twin. In theory, such surveillance would be useful in guiding obstetricians as to when intervention may be necessary, however evidence is lacking regarding whether intervening early (before signs of heart failure/polyhydramnios) is more beneficial and would improve outcomes. In the context of Canadian healthcare, the distances that may exist between the patient and her local unit and the distances between referring sites and fetal therapy centres further compound these issues, rendering weekly ultrasound surveillance and expectant management problematic in some cases.

RFA is the technique we used in this case and is a relatively new minimally invasive, percutaneous therapy for use in TRAP sequence pregnancies, with a reported survival rate of up to 94% [14,15]. Radiofrequency devices use progressively increasing high-frequency alternating current to induce temperature changes which cause coagulation and obliteration of blood flow to the acardiac fetus [16]. In this technique, injury to the co-twin and surrounding tissues is avoided as energy from the radiofrequency device is applied to the tip only after deployment into the desired region [7,17]. Though survival rates remain comparable between cord occlusion and intrafetal techniques, intrafetal RFA is associated with later median gestational age at delivery, lower rates of technical failure, lower rates of premature delivery or rupture of membranes before 32 weeks, and higher rates of pump twin survival following complete cessation of blood flow to the acardiac twin when compared with techniques targeting the umbilical cord [4,7] (Table 1). Furthermore, because it is a 'needle' technique not requiring insertion of large trocars, RFA is feasible in early pregnancy.

Prior experience with early amniocentesis suggested an increased risk of miscarriage due to premature membrane rupture with interventions performed before the obliteration of the coelomic cavity. For this reason, intrauterine interventions have typically been delayed until 16 weeks gestation and onwards. However there is very little evidence that early intervention with RFA carries greater risk. A study by Lewi et al. questioned the policy of prophylactic intervention at 16-18 weeks (the protocol followed by many centres), when they reported that 33% of TRAP cases result in spontaneous demise of the pump twin by 18 weeks of gestation [2].

Studies evaluating surviving pump twins have reported that interventions initiated after evidence of cardiac decompensation develops have a higher risk of cardiac complications and less favourable neurological outcomes [4]. Therefore, prophylactic intervention before 16 weeks may be beneficial in reducing fetal morbidity and optimizing intact pump twin survival.

With the introduction of the 11^{+0} to 13^{+6} week scans to screen for chromosomal abnormalities, the diagnosis of TRAP sequence in the first trimester is becoming increasingly more common [3]. There have been two recently published reports of successful intervention prior to 16 weeks. Cabassa et al. reported a monochorionic monoamniotic TRAP sequence managed with selective reduction by RFA performed at 14^{+1} weeks gestation. The fetus in their case was born preterm at 35^{+3} weeks gestation due to growth restriction, but whether this may have resulted from the RFA procedure was not discussed [18]. Paramasivam et al. reported a successful RFA intervention performed at 15 weeks gestation that resulted in a healthy infant born at 38 weeks [19]. These three cases highlight the questions resulting from early diagnosis and suggest that intervention prior to 16 weeks can be a safe and effective option when managing TRAP sequence pregnancy.

Our case contributes to a growing number of reports supporting the efficacy, safety, and potential necessity, of early intervention (prior to 16 weeks) for this complication of pregnancy. However, the evidence regarding the optimal method and timing of intervention is too small to definitively guide practice. Only two other case reports exist in the literature reporting intervention times prior to 16 weeks which may suggest a potential publication bias with negative results being

Study	n	Type	GA at RFA (weeks)	GA at delivery (weeks)	PTB <32 weeks	Survival of pump twin
Lee et al. [12]	98	81 MCDA 6 MCMA 11 triplets (5 DCTA, 6 MCTA)	20.2 +/- 2.4	33.4 overall 36.0 for survivors	16 IUFD 4 neonatal deaths	78/98 (80%)
Argoti et al.[18]	1	MCTA	23+4	31+5	PPROM 31wks	2/2 (100%)
Weichert et al. [19]	1	MC	23+2	38+4	26+4 preterm labour	1/1 (100%)
Cabassa et al. [17]	7	MCDA (6) MCMA (1)	17+3 (14+1 to 23+1)	33+0 (31+0 to 39+5)	1 IUFD 4 PPROM at 28 wks (21+4-31) 4/5 PTB	5/7 (71%)
Bebbington et al. [10]	18	MC	20.2+/-2.2	Median 33.0 (23.4-38.9)	13.7% PPROM Avg age 26.6+/-7, 75% before 32 weeks	14/18 (78%)
Roman et al. [9]	6	Triplets (2)	Not reported	Not reported	0	7/8 (88%)
Paramasivam et al. [11]	5	MCDA	Median 18 weeks (15 to 21)	Median 36 (24 to 41)	1 IUFD	4/5 (80%)
Jelin, et al. [1] only considered sTRAP (acardiac:pump weight <50%)	7	MCDA	Not reported	36.4 (+/-3.8)	0	7/7 (100%)
Livingston et al. [13]	13	MC (12), amnionicity not reported	21 (17-24)	37 (26-39)	1 IUFD 10 PTB <32 wks (PPROM)	12/13 (94%)
Lee et al. [15]	29	MCDA (26) MCMA(2) Triplets (1)	Not reported	34.8 overall 35.9 in MCDA	8/26 MCDA before 37 weeks	25/30 (86%)
Hirose et al. [20]	1	Not reported	27	32	0	1/1 (100%)
Tsao et al. [16]	13	MCDA	20.7	36.2	2/13	12/13 (92%)

GA: Gestational Age; RFA: Radiofrequency Ablation; PTB: Preterm Birth; MCDA: Monochorionic Diamniotic; MCMA: Monochorionic Monoamniotic; DCTA: Dichorionic Triamniotic; MCTA: Monochorionic Triamniotic; IUFD: Intrauterine Fetal Death; MC: Monochorionic

Table 1: Studies reporting twin reversed arterial perfusion sequence cases treated with intrafetal radiofrequency ablation.

underreported. In addition, two of the largest series, published by Lee et al. and Bebbington et al. including 29 and 18 cases, respectively, failed to discuss the timing of RFA procedures in their cohort [12]. Future studies allowing for detailed analysis of gestational age at the time of the procedure and subsequent birth outcomes would be beneficial.

There is a need for further study with larger samples to investigate the appropriate management of TRAP sequence. The North American Fetal Therapy Network's (NAFTNet) series published earlier this year by Lee et al. included 98 cases from 12 centres across North America and demonstrated the value of multicentre reviews [12]. Such multicentre reviews will facilitate incorporation of cases where intervention was performed before 16 weeks to allow direct comparison with cases where intervention occurred later in gestation and aid in determining the optimal timing for intervention. With the potential for larger sample sizes, randomized controlled trials should be initiated.

Recent evidence has also suggested that amnionicity may be a more valuable indicator of neonatal outcome in TRAP sequence than timing of the intervention [12]. This warrants further investigation and raises the question of whether monoamniotic cases should be managed differently than the more common monochorionic diamniotic cases [21].

In addition to determining the optimal timing for treatment of pregnancies complicated by TRAP sequence, it is hoped that future studies will also elucidate the best modality for this treatment. Recent reports have suggested that interstitial laser ablation of acardiac vessels is an effective and safe treatment which demonstrated improved outcomes in cases treated early in pregnancy when compared to cases managed conservatively [23,24]. Most recently, a novel non-invasive technique has been reported by Okai et al. [25]. In this method, High-Intensity Focused Ultrasound (HIFU) was used to stop blood flow to the acardiac fetus in a TRAP sequence pregnancy. Although at present there is extremely limited experience with this technology in human pregnancy, the concept of non-invasive therapy is one that deserves further development and research.

Conclusion

Although there is some evidence suggesting early intervention in TRAP sequence is associated with increased rates of fetal demise and premature birth, delayed or expectant management is associated with a high chance of pump twin death prior to18 weeks as well as an increased risk of adverse neurological outcomes. Advances in technology, such as the RFA procedure appear to have favourable outcomes with reduced procedure-related risk and supports early intervention for the treatment of TRAP sequence. Reports of successful, uncomplicated treatment with RFA at or before 15 weeks gestation is encouraging for management of cases diagnosed in the first trimester. This case contributes to a growing body of evidence demonstrating the potential benefits and safety of early intervention with RFA in the management of TRAP sequence.

Acknowledgement

We would like to thank the patient whose pregnancy is described here for her permission to publish her history.

We would also like to thank Pamela Chan for the illustration describing the TRAP sequence physiology.

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