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Sonography

Twin reversed arterial perfusion (TRAP) sequence: A case report and a brief literature review ☆

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ABSTRACT

Twin reversed arterial perfusion (TRAP) sequence is rare in monochorionic twin pregnancies. TRAP sequence is distinct from other multifetal pregnancies in that one of the twins has normal anatomy while the other twin has a varied amount of characteristic abnormal features. In the literature, mortality is reported 100% in the abnormal twin. We report 1 case of TRAP sequence at our institution in which the diagnosis of TRAP sequence was missed in the first trimester at another hospital. The patient, a 33-year-old G1P0A0, did not have any follow-up after her first scan until the routine second-trimester ultrasound at our institution. Both the radiologist and the sonographer did not appreciate the differential diagnosis of TRAP sequence in their clinical decision-making. The TRAP diagnosis was established after the ultrasound performed at the fetal assessment unit in our hospital. Radiofrequency ablation (RFA) procedure was performed to give the normal twin a chance to survive, but unfortunately, the prognosis was poor in this case. We conclude that diagnosing a TRAP sequence is very important early in the pregnancy for a positive outcome in the normal twin. A robust collaboration among radiologists and obstetricians is vital for the best outcome of the normal twin.

Introduction

Acardiac twinning or the modern term "Twin reversed arterial perfusion" sequence is not a new clinical finding. Since the first description of the acardiac twins by Benedetti and Benedictus in 1533 & 1539, respectively, a lot has been published in modern times in relation to this pathology [1,2,33,39]. Geoffroy de Saint-Hilaire used the term "Acardia" for the first time and fully described it in 1838 [2,4,8,18]. Van Allen et al. suggested the term Twin reversed arterial perfusion for all acardiac fetuses in 1983 [2,9]. As the name suggests, one of the

Abbreviations: TRAP, Twin Reversed Arterial Perfusion sequence; DVD, Ductus Venosus Doppler; RFA, Radiofrequency Ablation; PPROM, Preterm Premature Rupture of Membrane; UA, Umbilical arteries.

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twins has no functional heart hence the term associated with the pathology. Schatz (1899) divided the acardiac twins into 2 broad categories: one without any sign of cardiac tissue and the second category having some rudimentary cardiac activity type. The former was referred to as holoacardius and the latter as hemiacardius [6]. Das (1902) further categorized TRAP sequence classification into 4 groups still in use in modern literature [7]. These are as follows:

1. Acardius acephalus: absence of head, upper extremities, and thoracic organs with fair development of lower extremities and pelvis; is the most common of all the 4 types.
2. Acardius amorphous: unrecognizable human fetal features. It presents as a blob of tissue with umbilical vessels.
3. Acardius acormus: The rarest form of arcadia known (5% incidence). The head with umbilical vessels is present.
4. Acardius anceps: this type of acardia has a partially developed head and/or face with extremities plus the abdomen and pelvis. Acardia anceps might be regarded as the most advanced type of acardius relative to the other three [29,39].

The fifth category of acardia called acardius myelacephalus, was suggested by Simonds & Gowen (1925). Acardius myelacephalus refers to a partially developed head with identifiable upper limbs plus and/or minus some nervous tissue [8,13]. In modern times, Lehr, and Dire (1978) are often credited in the literature for grayscale imaging of the acardiac twin in utero [10]. Pretorius et al. published an article in 1988 in which they demonstrated the retrograde flow of arterial blood by colour doppler. However, the original idea of the reversed flow of arterial blood in the TRAP sequence was floated by Claudius, and Strauss [2,11,34]

Incidence

Gillim & Hendricks (1953) suggested the incidence of TRAP sequence to be 1 in 35000 births to 1/50000 births overall [3]. Kappelman (1944) reported that the incidence of TRAP is 1% in all monochorionic pregnancies [4]. Van Allen et al. (1983) believed that the TRAP sequence incidence is underestimated [9]. Gemert et al. (2015) recently postulated new incidence numbers for the TRAP sequence. The authors reported that the incidence of TRAP could be 2.6% in all monochorionic pregnancies or 1 in every 9500-11000 pregnancies [5]. Miller (2021) and Quaas (2021) suggested that the incidence of TRAP sequence could be higher due to early detection of the condition by first-trimester scan and the increasing use of assisted reproductive technology [23,55]. Wehypothesize that the TRAP sequence incidence might be higher in countries with high fertility and twin pregnancy rates, ie Niger, Nigeria and some central African nations [12,35,36,45]

Pathophysiology

Kahler (1789) was the first to suggest the role of abnormal umbilical vascular connections in one of the acardiac fetuses in triplet pregnancy [2,52]. Schatz and Claudius are some pioneer researchers who observed the abnormal vascular connections and reversal of circulation in the umbilical vessels in this condition [2,34,39,20]. Ahlfeld (1879) also suggested the role of vascular arterial anastomosis in the placenta as the basis of the pathophysiological process in acardiac twinning [2,13,24]. Schatz (1900) also suggested that the reversal of circulation could explain many anomalies in these fetuses [6]. In modern times some authors have provided further evidence that the pump twin retrogradely perfuses the other twin with deoxygenated blood to the abdominal aorta, hence preferentially receiving a better blood supply [9,14,19]. This results in the lower part of the body developing better than the upper part, including the heart [16]. Benirschke (1977) postulated that the pathology of acardiac twins is not due to genetic disorders, but it appears to be related to the vascular anastomoses in the placenta [20]. Langlotz et al. (1991) postulated that cardiac morphogenesis or atrophy may be due to reversed arterial blood flow and hemodynamic stress-related pathophysiology [37]. This might explain why acardius acephalus is the most common of the 4 types of classification of TRAP. Benirschke (2009) mentioned that the unequal splitting process in monozygotic twins might be the embryological reason for acardiac and twin to twin syndrome [17]. In a case series of 14 cases, Van Allen (1983) documented that 40% of the acardiac twin pregnancies belong to monoamniotic-monochorionic (MCMA), and 60% to MCDA type of chorionicity [9]. The authors reported 2 conditions vital to the pathogenesis of TRAP sequence: first, a close approximation of umbilical arteries of the twins on the placenta, and second, discordant growth of twins, which may facilitate the reversal of arterial blood flow in the disadvantaged twin. The authors further stated that the impairment in proper vasculature is the cause of abrupt morphogenesis in TRAP sequence [9] . Sepulveda et al. (1993) further reported that the increase in arterial pressure in one twin might lead to a reversal of arterial flow in the other twin, thereby contributing to TRAP sequence [21]. Sullivan et al. (2003) suggested that the high perinatal mortality rate in acardiac twinning is because of the increased demand placed on the normal twin to perfuse the acardiac twin [15]. Moore et al. (1990) noted the following perinatal complications with acardiac twinning: CHF, polyhydramnios, and preterm delivery [16].

Here we present a case report of a 33-year-old female referred to our hospital for a routine second-trimester ultrasound scan. For this case report, we define a normal twin as Twin A, and an anomalous twin as Twin B.

Case report

A 33-year-old G1P0A0 female was referred to our hospital for a routine 20-week (2nd trimester) ultrasound scan. No apparent concerns were noted in the history obtained by the sonographer. The patient was previously scanned in another hospital in the vicinity during the first trimester for spotting complaints. The sonographer at that time noted normal heart rate and sonographic age consistent with menstrual age in Twin A (Figs. 1A and 1B). The sonographer also reported an abnormal structure adjacent to the normal viable twin in the gestational sac (Figs.1C and 1D). The radiologist did not mention any sonographic impression in the radiology report. The radiologist did not appreciate any abnormality in this first-trimester scan. As a result, timely diagnosis of a potential obstetrical abnor-

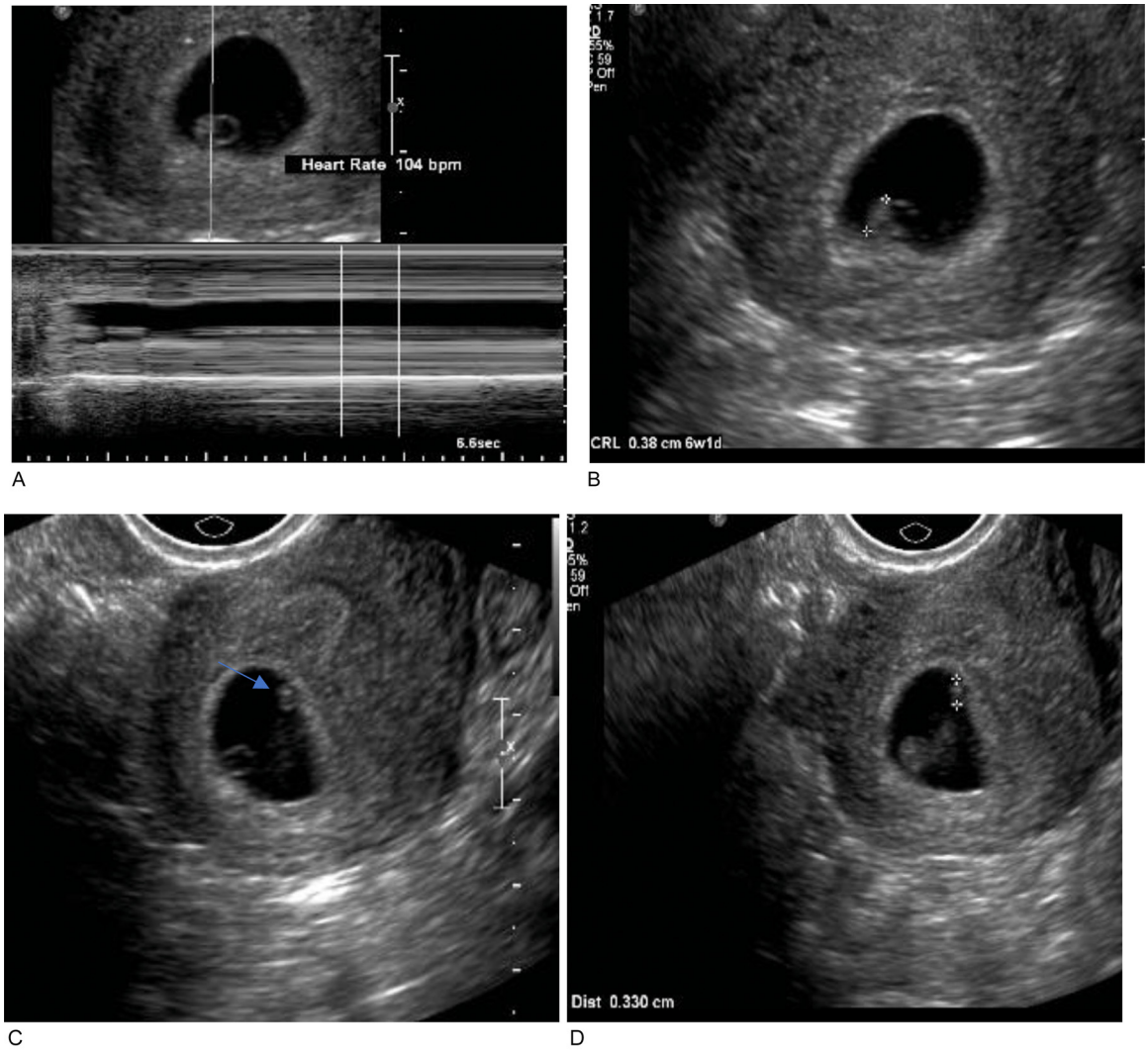


Fig. 1 – (A) Twin A with yolk sac & normal HR for the first trimester. (B) Twin A CRL = 3.8 mm corresponding to 6 weeks 1 day. (C) Twin B (arrow) alongside Twin A. (D) Twin B = maximum length is 3.3 mm

mality (TRAP sequence in this case) was missed in the first trimester.

Routine second-trimester obstetrical scans are typically performed at 20 weeks of gestation in our health region. The patient was referred to our institution for a routine scan in the second trimester by her family physician.

We noted 2 intrauterine fetuses; one appeared to be a healthy normal fetus (Twin A) while the other was felt to be a grossly anomalous variant of this twin pregnancy (Twin B). The sonographer noted normal anatomic development in twin A except a 2-vessel cord (Fig. 2A). All 4 chambers of the heart were normal sonographically, and the FHR measured by M-mode was 153 bpm (Fig. 2B). The patient did not want to know the gender of the fetus; hence it was not documented.

As per the Hadlock package on IU22, this twin's gestational age came at 20 weeks 6 days, which was 20 weeks 5days by LMP, and 20 weeks 4days by extrapolation from the first-trimester scan. As per the Hadlock package, the fetal weight of twin A was 375 gm (Fig. 3A).

The Amniotic fluid volume was relatively normal but borderline high, measured at about 8 cm (Fig. 3B).

Twin B was abnormal with gross defects in organogenesis. The spine was seen in the sagittal section, but the cervical, and sacral regions were not appreciated well on grayscale imaging (Fig. 5C). A small for gestational age, a skull was visualized on a 2 D ultrasound scan (Figs. 6A and 6C). No definitive brain tissue was identified in the images. A large amount of free fluid was seen in the thoracic as well as the abdominal cavity (Figs. 5B and 5D). No limbs were identified sonographically. Also, during the scan, we could not find a definitive membrane separating the 2 twins; hence sonographically, we thought this twin pregnancy to fall under the MCMA category. The ultrasound performed at fetal assessment and the pathology report later disapproved our impression, and the twin pregnancy was confirmed to be MCDA type. The radiologist on-site noted fetal cardiac movements and took appropriate still images & video and/or cine clips (Fig. 6B). Cine clips nicely showed 3 anomalous cardiac chambers beating synchronously. Due to the hy-

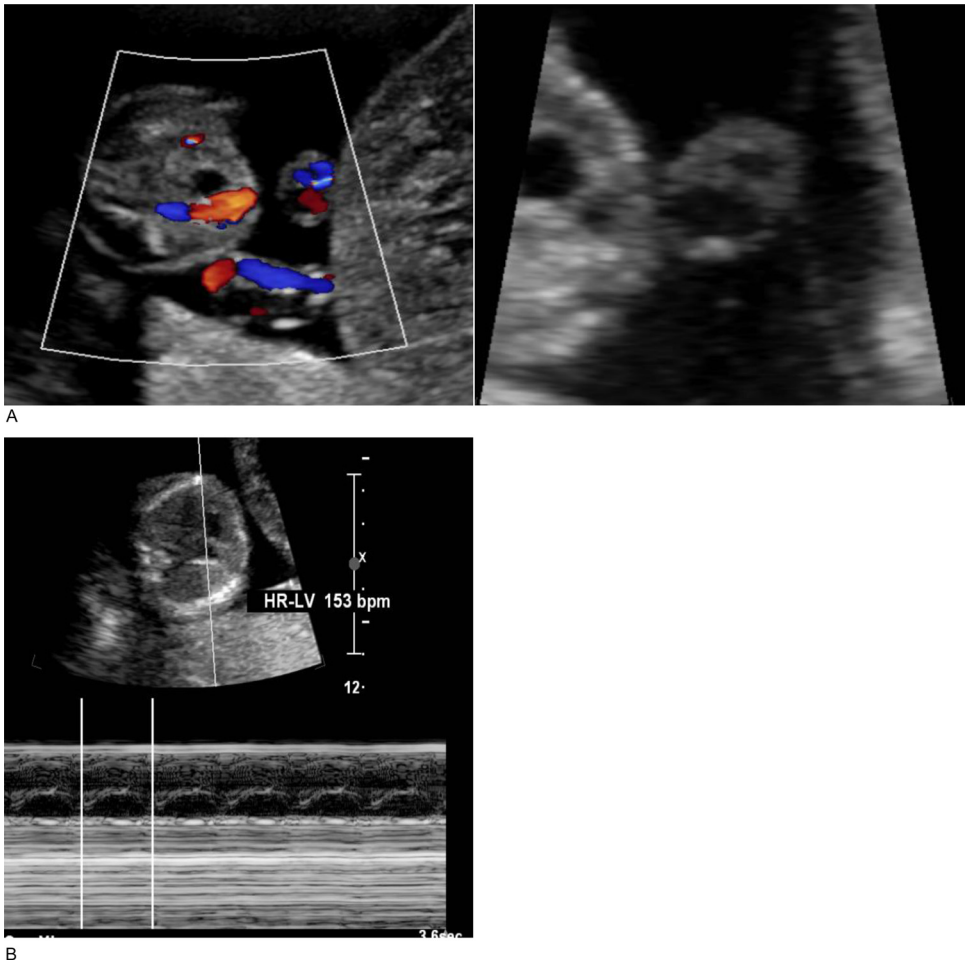


Fig. 2 – (A) Single umbilical artery demonstrated by color doppler and in transverse grayscale imaging. (B) Twin A normal heart rate by M-mode.

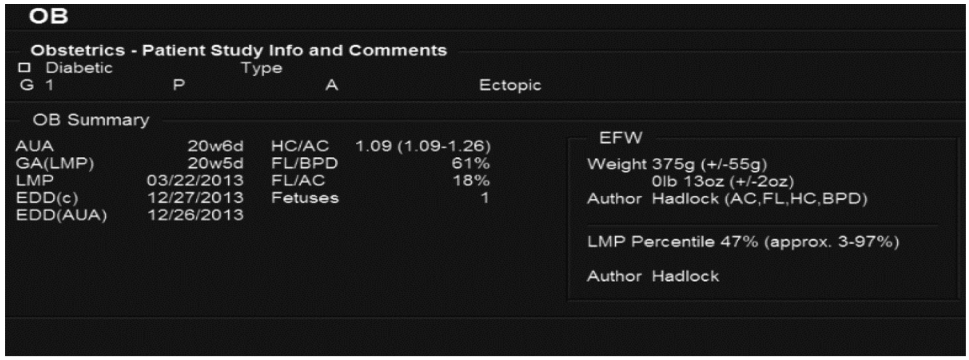
dropic nature of this abnormal twin, no definitive cord insertion into twin B was identified in this pathologic variant. The radiologist and the sonographer never saw this pathology in their career. They hence did not perform a full sonographic color doppler assessment on the anomalous tw↑in to properly diagnose the TRAP sequence.

Considering the gross pathology in the anomalous twin, the patient was referred to Obstetrics & Gynecology for further management. The patient was scanned in the fetal assessment unit (FAU) on the same day. Twin A was reported to have the middle cerebral artery velocity of 36-42 cm/sec & normal UA Doppler. Ductus Venosus Doppler is sometimes used to evaluate the health of the normal twin's heart status [32]. The Ductus venosus Doppler in twin A at the fetal assessment unit revealed a reversed flow pattern in the "a" wave. Kennedy & Woodward(2019) reported that "a" - wave reversal in DVD is a vital sign of impaired cardiac performance in the normal twin [35].

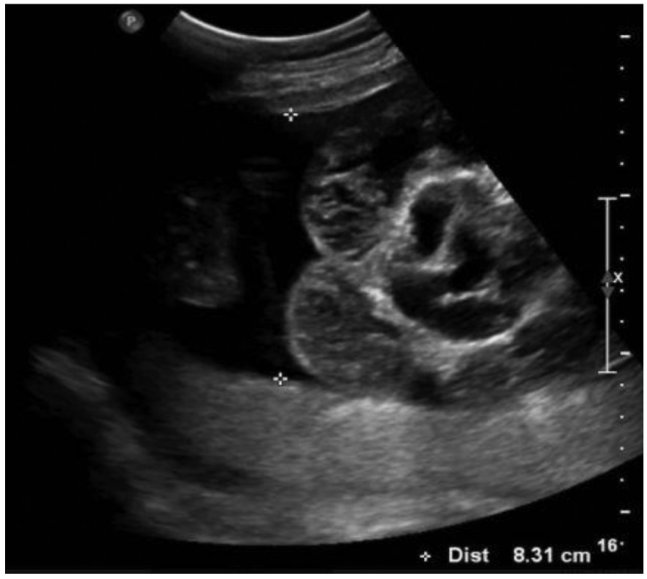
For Twin B, FAU documented the size of the head corresponding to a 13-week-old fetus without any signs of brain tissue (Figs. 6A and C). The chest and abdomen were grossly filled with fluid plus massive edema of the soft tissues (Fig. 5B). The fetal HR for this twin was recorded at 110 bpm. Umbilical artery doppler interrogation revealed blood flow from healthy twin A entering twin B via UA, thereby confirming the diagnosis of TRAP sequence in utero. The patient was informed of the prognosis, and explained the management and/or intervention in this pregnancy. The obstetrician recommended radiofrequency ablation in the acardiac twin to reduce the chance of cardiac failure in the normal twin. Informed consent was obtained from the patient for RFA.

Three days after the recommendation for RFA, the patient was scheduled for this procedure at a major tertiary hospital in the province. During the procedure, the obstetrician aspirated 129 ccs of clear fluid from the abdominal cavity of twin B, resulting in an appreciation of 2 umbilical arteries coming into contact with the umbilical vein. Because of this finding, twin B was felt to have 3-vessel cords. With the help of ultrasound, the obstetrician deployed the tynes of the RFA probe on the umbilical vessels of Twin B to ablate the vessels. RFA deployed 30W to 50W of energy at regular intervals to obliterate the umbilical artery in the anomalous twin meticulously. The procedure was regarded as a success when no blood flow was elucidated in the umbilical vessels of the acardiac twin.

The next day after the RFA procedure, PPROM was confirmed, and suspected of being from the anomalous twin's amniotic sac since there was adequate amniotic fluid around



A



B

Fig. 3 – Amniotoc fluid volume.

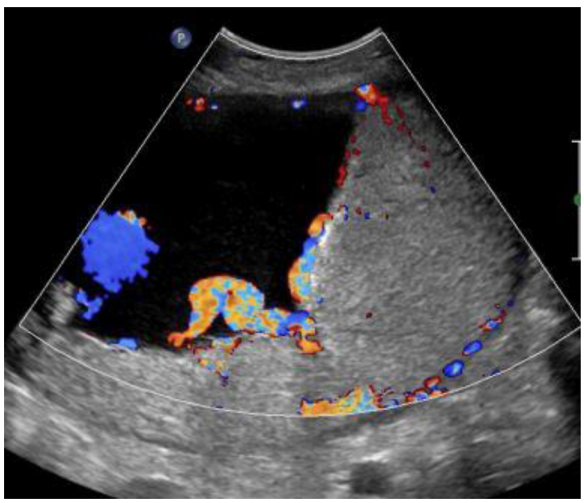


Fig. 4 – The placenta was placed posterolaterally on the uterine wall and the chorionicity was sonographically determined to be monochorionic. (Figs. 4 and 6A).

twin A. Three days after the RFA procedure, the patient started feeling sudden cramping in the pelvic region plus felt a sudden gush of fluid per vagina. The obstetrician performed a bedside ultrasound immediately, which revealed oligohydramnios in twin A. Later on, now the PPROM was confirmed from the twin A amniotic sac. The patient subsequently delivered both twins on the same night. Apgar's score on twin A was 4 at 1 minute and 4 at 5 minutes. The twin A died 2 hours after the delivery.

Pathology report

The pathologist confirmed the MCDA pregnancy based on the placental specimen. The autopsy was performed on the twins, and the pathologist further confirmed the diagnosis of Twin Reversed Arterial Perfusion (TRAP). Following are the excerpts noted from the pathology report:

Twin A: no abnormal anatomy elucidated except the 2-vessel cord.

Twin B: No segment of the umbilical cord was identified on gross examination. Head and body seem to be fused. The specimen revealed the absence of left upper extremity and rudimentary right upper extremity plus 2 lower extremities.

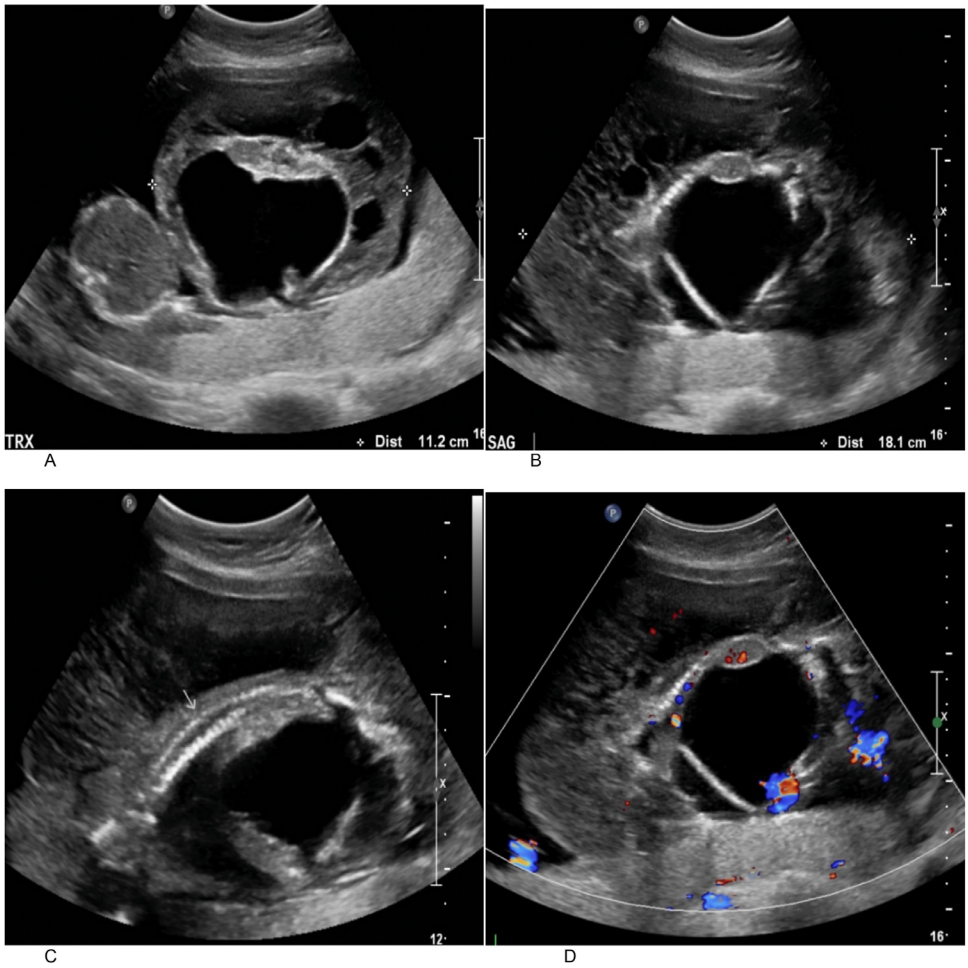


Fig. 5 – (A) Transverse section of Twin B. Twin A is to the left of the image. Also note the posterior lying placenta (B) Sagittal section of Twin B. Note the fluid-filled abdomen and thoracic cavity. . . Sagittal spine is partially visible in this view. (C) Twin B in grayscale imaging. Note the sagittal spine with lumbar & thoracic vertebra relatively well seen in this plane of section. (D) Colour doppler on twin B.

The pathologist also identified orifices for possible mouth and anus. Gender was not seen on gross examination. The pathologist also identified a defect on the anterior aspect of the abdomen measuring 3.2 × 2.9 cm, exposing some of the abdominal contents. The pathologist report did not mention if it was a case of gastroschisis or omphalocele. A baby infantogram was also performed on this specimen, consistent with the skeletal deformities described above (Fig. 7). Due to technical reasons, the gross pathologic images of the TRAP sequence twins were unobtainable.

Genetics

Molecular genetic tests were done to detect aneuploidy on both twins. Elucigene QST*Rplus v kit was used to detect the most common autosomal trisomies, namely trisomy 13(Patau syndrome), trisomy 18 (Edwards syndrome), trisomy21 (Down syndrome), and sex chromosomal aneuploidies [51]. The genetic tests also identified both twins to be genotypically female (46,XX), which further points toward the monozygotic nature of this twin pregnancy. Van Allen et al. (1983) suggested that the recurrence risk of acardiac twin pregnancy be on the order of 1 in 10000 monozygotic(MZ) twin pregnancies [9]. The authors suggested the use of ultrasound to detect future MZ twins and the potential occurrence of perfused twins in these patients [9]

Discussion

In our department, as per records, this was the first of its kind pathology in the last decade. TRAP is a rare and most severe form of twin-to-twin transfusion syndrome (TTTS) [19]. Based on the second-trimester routine ultrasound scan, fetal assessment scans and the pathology report, we believe our twin B belongs to the hemiacardius, and acardius anceps category [7]. The imaging professionals should always have this diagnosis as their top differential if they see an abnormal developing fetus alongside a normal twin in the preg-

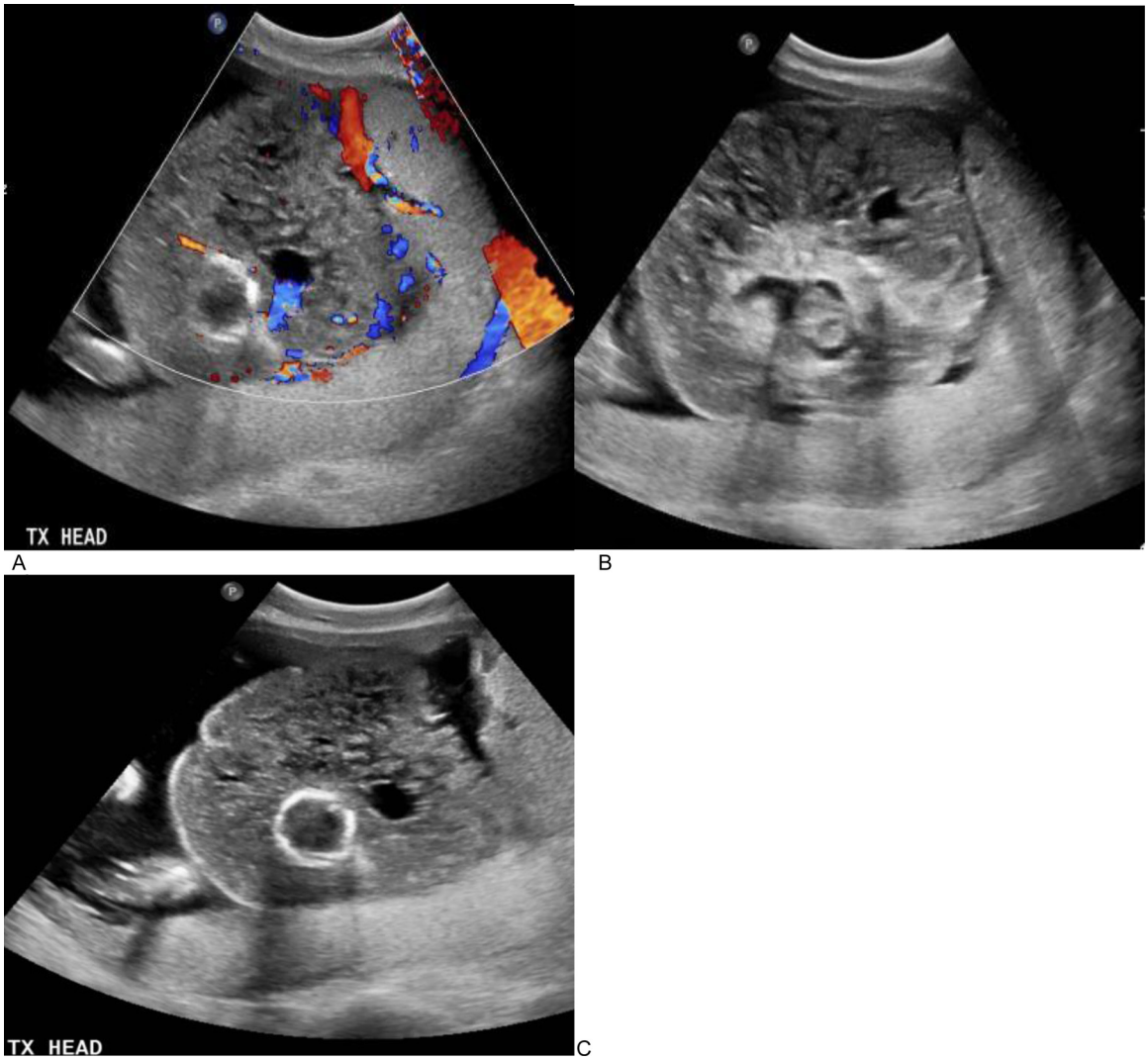


Fig. 6 – (A) Twin B Transverse Head. Note the posterior and/or lateral placenta. (B) Twin B Rudimentary heart in grayscale. (C) Maldeveloped head with ossification of skull.

nancy [22,50]. The other differential diagnosis for TRAP is Intrauterine fetal death(IUFD) [21,25], fetus papyraceus [9], vanishing twin, and TTTS [19,28]. Unfortunately, in our case, the radiologist did not report the findings of an abnormal structure in the gestational sac alongside the normal crown-rump length in the first trimester, even though it was mentioned in the sonographic technical impression. We speculate that if appropriate documentation of this abnormal structure was mentioned in the first-trimester scan, it would have led to a better obstetrical outcome for the normal twin. For instance, Donnenfeld et al. (1991) suggest bi-weekly fetal echocardiography with doppler interrogation to assess the pump and/or normal twin's cardiac functionality once the diagnosis of TRAP is made [38].The diagnosis of TRAP sequence requires adequate knowledge of pathology and the sonographic interpretation of the condition. The radiologist and/or sonographer must be diligent in documenting the sonographic features of this rare entity [22,50]. Sonographic documentation of reverse flow in the umbilical arteries is a pathognomonic feature of TRAP sequence [27,28]. An expedient diagnosis of TRAP by ultrasound must be made to provide enough opportunity for the obstetric team to come up with the treatment and management options for the overall outcome of the pregnancy [50,54]. A teamwork effort between obstetricians, radiologists and sonographers is essential to properly document the progression of the TRAP pregnancy, especially if the decision to delay immediate intervention is required.

In the literature, the weight comparison between the anomalous twin, and the normal twin is used as a rough estimate for predicting the outcome of the pregnancy. Moore et al. (1990) came up with a second-order regression equation to deduce the weight (in gm) of the anomalous twin: - 1.66 (maximum Length) + 1.2 (Max. Length) [2,16]. The authors reported that the pregnancy outcome is favorable if the ratio of abnormal to normal twins in TRAP is <70% and worse if it is more than 70%. Sepulveda et al. (1993) also believed that the twin weight ratio is an essential prognostic factor for the outcome of the TRAP pregnancy [21]. If we were to extrapolate this concept in our case, the estimated weight of our anoma-

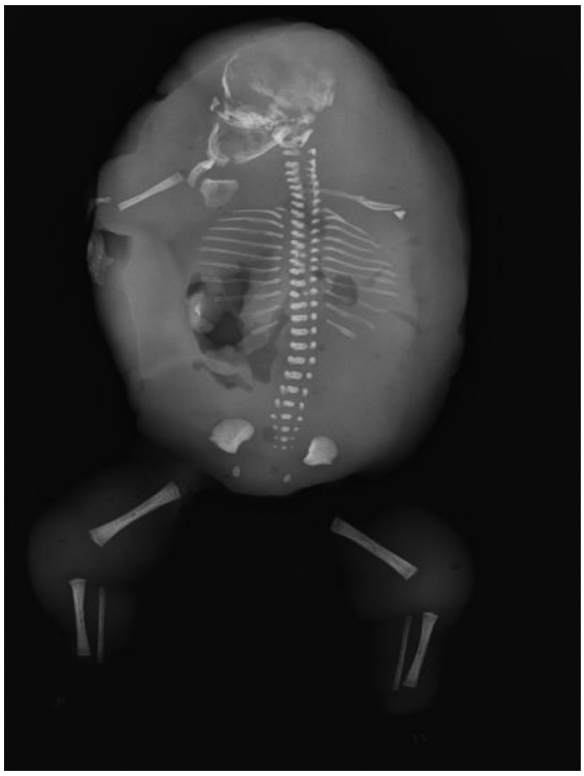


Fig. 7 – X-ray or infantogram shows Right Arm, right and left lower extremity. Note the Right humerus, absent left humerus, presence of both right and left femur plus tibia and fibula in this infantogram.

lous twin based on a maximum length of 18 cm was approximately 359 gm. As per the Hadlock package, twin A measured 375 gm (Fig. 3A), yielding a 0.96 or 96% ratio. Hence theoretically, based on Moore's equation, this TRAP sequence pregnancy had a worse prognosis for the outcome in twin A.

Malone & D'Alton (2000) suggested expectant management for TRAP sequence if the weight ratio is <0.70, echocardiographic evidence of absence of heart failure in pump twin, and adequate AFV status. The authors suggested weekly sonographic surveillance if the goal is to follow expectant management. Sullivan et al. (2003) also concluded that expectant management could be considered with appropriate antenatal surveillance [26]. Some authors suggest early intervention for a better perinatal outcome overall [42,46,47]. Currently, there does not exist any consensus in regards to timing for intervention in this pathology. In the literature, some authors are proponents of expectant management if the prognostic features of the TRAP sequence are manageable [53]. In 2016, a multicenter, open-label, randomized controlled trial was initiated to elucidate if the early intervention (12-14 weeks; study group) has a better pregnancy outcome relative to later intervention (16-19 weeks; control group). The result of this study is expected to be available to the public by mid of 2022 [30].

Some authors believe that if the prognostic characteristics are worrisome, ie CHF in normal twin, polyhydramnios, twin weight ratio (acardiac and/or normal twin), aneuploidy and hydrops fetalis, aggressive early first-trimester intervention is recommended [20,25,40]. Plat et al. (1983) were the first authors to suggest an interventional approach to occlude the umbilical vessels of the arcadia twin [31]. Several treatment options are available to manage the TRAP pregnancy, namely alcohol embolization, radiofrequency ablation(RFA), ligation, microwave ablation, thermocoagulation, laser coagulation & high intensity focused ultrasound [29,42,43,44]. Some authors recently reported that out of all the modern techniques to treat TRAP, RFA is the most effective procedure with a high safety index [23,29,40,41]. The use of ultrasound is vital in performing RFA to target the probe and/or tynes close to the target tissue of interest. Regardless of the several treatment options available, the prognosis of TRAP pregnancy is not very encouraging. The anomalous twin is incompatible with life in an ex-utero environment owing to its parasitic reliance on the blood supply from the normal twin. The mortality is 100% in these unfortunate twins [49,54]. The normal twin has a perinatal mortality rate of approximately 50%-55% based on the literature review [9,16,48,49,54,56]. Sullivan et al. (2003) reported that the pump twin (normal twin) has high perinatal mortality owing to increase hemodynamic stress placed on the heart to perfuse the anomalous twin [26].

Conclusion

Twin Reversed Arterial Perfusion (TRAP) is a rare pathologic obstetrical condition. Because of its rare incidence, many radiologists, sonographers and obstetricians do not see this condition often in their practice. Therefore, it becomes crucial to understand and document this pathology with due diligence for the management and care of patients, especially when 50% of the time, the normal twin could be saved at the expense of the anomalous twin. Any morphologically anomalous fetal tissue besides the normal growing twin should be investigated scrupulously by ultrasound. Imaging professionals must be knowledgeable about this rare obstetrical phenomenon as it can define the management of the pregnancy as a whole. A strong and prosperous collaboration between radiologists and obstetricians is essential for the better outcome of TRAP sequence once the medical condition is diagnosed in utero by ultrasound.

Patient consent

Written informed consent was obtained from the patient on December 3, 2021 for the purpose of this case study. Case Study received formal approval from the Research Ethics and compliance committee (affiliated with the University of Manitoba) for publication, Dated: February 10, 2022. Ethics Reference Number: HS25395 (H2022:081).

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