

CASE REPORT

The TRAP (twin reversed arterial perfusion) sequence – case presentation

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Abstract

We present a particular case of TRAP (twin reversed arterial perfusion) syndrome, which has a very rarely association of the simultaneous existence of a rudimentary malformed heart and brain, and also other malformations like abdominal wall abnormality, absent bladder with present kidneys, and absence of the lungs, which appear only in a few cases on the receptor twin from this sequence, malformations incompatible with life. A Caucasian 26-year-old pregnant woman, at the first pregnancy, with a monochorionic-diamniotic pregnancy, 26 weeks of gestation was referred to our hospital, for polyhydramnios. The patient delivered a living female newborn, weighing 950 g, with an Apgar score of 2 at one minute – the donor fetus and a second female newborn with multiple malformations, no signs of life and who weighed 2300 g – the receptor fetus. The anatomopathological examination confirmed the TRAP sequence associated with severe facial dysmorphism, bilateral phocomelia and cardiac malformations (rudimentary hypoplastic, univentricular) and a vascular anastomosis between the two umbilical cords. Anemia and cardiac complications which can lead to cardiac failure, appear early during pregnancy and caused the death of the pumping twin. We emphasize that in our case of TRAP sequence, the ultrasound examination established the diagnosis of the syndrome with high accuracy. Therefore, we can conclude that the existence of a rudimentary heart and a vascular anastomosis between the two umbilical cords supports the apparition of TRAP sequence. The early diagnosis of this pathology, the observation of the pregnancy with the help of weekly ultrasounds and the intrauterine interventions can increase the survival chances of the donor fetus from the TRAP sequence.

Keywords: particular TRAP sequence, rudimentary/absent heart, early diagnosis, other associated malformations.

Introduction

The TRAP (twin reversed arterial perfusion) sequence is a rare complication of the multiple monochorionic, mono- or diamniotic pregnancy, in which one of the twins has an absent heart or a rudimentary heart (or a non-functional one). This condition has been described as being the most severe malformation seen in humans. This malformation affects all body systems, which are invariably abnormal [1]. TRAP sequence has been described with a frequency of 1/35 000 pregnancies or 1% of monochorionic pregnancies [2, 3]. Out of a series of 36 TRAP sequences, only two were monoamniotic, the rest were diamniotic [4], other authors stating that 24% of the pregnancies were monoamniotic [5]. It is considered that the acardiac twin is like a parasite. The etiopathogenesis of this abnormality is explained by the presence of an arterio-arterial anastomosis or by dysmorphogenesis [6]. Cardiac dysmorphogenesis is supported by the trouble in organogenesis, a “cardiac regression sequence”. The arterio-arterial anastomosis is hold by the reversed blood flow from umbilical artery of the pump twin into the umbilical artery of the perfused twin, thereby by passing the placenta [7, 8].

The definition of the TRAP sequence was given by Van Allen *et al.* (1983) [9], who clarified the patho-

physiological aspects of the condition, which implied a reversed perfusion from pump to acardiac twin *via* single anastomosis. This single vein-to-vein or arterial-to-arterial connection is between the two cords or indirectly through the chorionic plate.

The acardiac twin, which has the development only in the lower part of his body, has a perfusion with hypoxic blood and the mortality is 100%. Usually, the pump twin is anatomically normal, but his survival is only about 50% and his dead is due to the heart failure or prematurity caused by polyhydramnios [9]. In our case too, the acardiac twin – the receptor was born dead and the second twin – the donor, died 10 days later due to the complications of prematurity.

The pathophysiology of this malformation is uncertain. According to the fetal blood flow, it can be seen that from the normal fetus – the donor, pass through the placenta, which has arterio-arterial anastomoses to umbilical artery low oxygen blood in the system blood of the acardiac twin – the receptor, creating a reverse arterial perfusion – TRAP sequence [10, 11]. The donor twin had to maintain the fetal blood flow, so that the heart of the pumping twin had to support his own blood flow and the one of the acardiac twin. Because there are arterio-arterial anastomoses the blood from the pumping twin to the receptor

twin can not pass through the capillary bed [10]. The perfusion will be with unoxygenated blood especially in the inferior part of the receptor twin and with a weak perfusion at the level of the superior part of the body, especially at the head [10]. Therefore, the acardiac twin has a good developed inferior part of the body and a lack of the development in the superior part of the body represented by anencephaly or holoprosencephaly, being like a parasite fetus [2].

Aim

Our paper aims to present a case of TRAP sequence, which is a particular one, because this case has a very rarely association of the simultaneous existence of a rudimentary malformed heart and brain. Moreover, other malformations like abdominal wall abnormality, absent bladder with present kidneys and absent of the lung are rarely associated with the abnormalities of the receptor twin from this sequence.

Case report

A Caucasian 26-year-old pregnant woman, at the first pregnancy, from the urban area, was referred from the territory to our third level maternity, for polyhydramnios. She had a monochorionic-diamniotic pregnancy, at 26 weeks of gestation and she was diagnosed with a polymalformative syndrome of one of the twins.

From the pregnancy history, we found out that the pregnancy was supervised in another regional hospital, with a diagnosis of multiple pregnancy complication. She was 27 weeks of her last menstrual period and the estimated gestational age was 26 weeks and two days. She had no history suggestive of viral or bacterial infections, no alcohol or drug ingestion during first trimester. She and her family had unremarkable medical history. Her family history was not contributory for twin pregnancy. There was no consanguinity. The amniocentesis of the pump twin had a normal karyotype, the last ultrasound being performed at 20 weeks of gestation. The patient did not show up to the periodic pregnancy check-ups after this age of pregnancy. According to the evolution of the pregnancy, we mention that any problems were found during the first and second trimester of pregnancy. A day before the admission in our hospital, the pregnant women presented to a regional hospital for rapid abdominal volume increase and dyspnea. Due to the presence of polyhydramnios, gestational age and the presence in our hospital of the neonatal intensive care unit, the patient was referred to our department.

At admission, clinical examination revealed that the patient presented a distended abdomen, with an abdominal circumference of 106 cm, elevated uterine basal tonus, active fetal movements and without any vaginal leakage of fluid or blood. Her vital signs were stable. She had no signs of labor at the admission. Vaginal examination revealed no cervical dilation, intact membranes, without uterine contractions. The presenting part was difficult to appreciate.

Laboratory finding did not reveal any changes: the blood count, the coagulogram and the urine exam had normal values.

A transabdominal ultrasound evaluation was done with a volumetric probe RAB/4–8 MHz with a Voluson Pro machine. At the ultrasound examination, we discovered a monochorionic-diamniotic pregnancy: polyhydramnios in the fetus with normal structure and biometry, signs of cardiac failure and severe anemia; the second fetus had multiple malformations, with multiple anechogenic cavities, surrounding a skull structure, a deformed spine and thorax (which were also very small for the patient's gestational age), a bicameral heart with episodes of mild bradycardia, an abdominal wall defect and a limb defect. The Doppler exam on the umbilical artery of the receptor twin indicates the presence of a reverse flow (Figures 1–4). Our diagnosis was the TRAP sequence.

The patient begun to present signs of labor a few hours after admission and due to the fetal position, she delivered through C-section a living female newborn, weighing 950 g, with an Apgar score of 2 at one minute and 8 at 10 minutes – the donor fetus. The second female newborn had amorphous upper torso and multiple malformations, no signs of life and weighed 2300 g – the receptor fetus (Figures 5 and 6) and well formed lower limbs.

During the macroscopic examination of the unique placenta, an anastomosis between the two umbilical cords was discovered, on its fetal side (Figure 7). The first and living newborn-donor fetus was resuscitated and transferred to the special care baby unit. She had no abnormalities, she was anemic (hemoglobin 8.5 g/dL), but deceased in her 10th day of life, in spite of all the intensive care which was instituted from the very beginning. The death was due to the complications of the prematurity based on the severe chronic anemia (death diagnosis – severe form of the acute respiratory distress syndrome, which required the administration of surfactant and invasive ventilator support, persistent pulmonary hypertension, left ventricular hypertrophy, anemia post-TRAP syndrome, intraventricular bilateral cerebral hemorrhage, cardiorespiratory arrest) and cardiac failure too.

The mother was discharged after the death of the second twin, on the 10th day in satisfactory condition.

We mention that the child's parents agreed with the report of the case and gave an informed consent for publication.

The patient was counseled in consensus with the international protocols, but the genetic examination was not performed because the patient declined this, despite adequate counseling.

The anatomopathological examination of the second newborn-receptor fetus confirmed the diagnosis of TRAP sequence. The autopsy of the first newborn – donor fetus did not find any other data in comparison with the death diagnosis.

The macroscopic description highlighted: severe facial dysmorphism (holoprosencephaly, cheiloschisis, anophthalmia, cystic hygroma), bilateral phocomelia, left equinovarus foot, subumbilical abdominal wall agenesis with a cystic protrusive peritoneal mass, cardiac malformations (rudimentary hypoplastic, univentricular, uniauricular heart with a present aorta from which the left pulmonary artery emerges, right pulmonary artery agenesis, inferior vena cava agenesis), right lung agenesis, left lung hypo-

plasia, hepatic agenesis, diffuse subcutaneous edema, present pancreas and kidneys, absent urinary bladder, fetal annexes with a normal histological aspect.

Microscopically description: immature lung, with signs of pulmonary atelectasis (Figure 8), the heart presenting all three layers: epicardium, myocardium, endocardium (Figure 9), the umbilical cord with a normal histological structure, immature kidney (Figure 10).

The particularity of the case

TRAP sequence is rarely associated with the simultaneous existence of a rudimentary heart, a malformed head and brain. Moreover, the abdominal wall abnormality, absent bladder with present kidneys, an absent lung are rarely described, associated to the abnormalities of the receptor twin from this sequence.

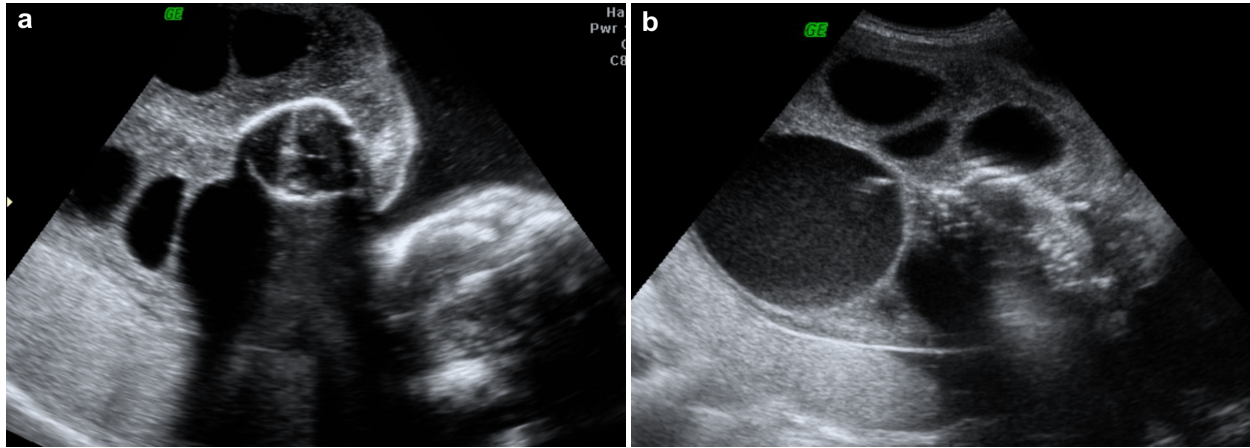


Figure 1 – (a and b) The echographic aspect of the receptor fetus with multiple anechogenic subtegumentary images skull (left) vertebral spine and hyperechogenic aspect of the thoracic cage (right).

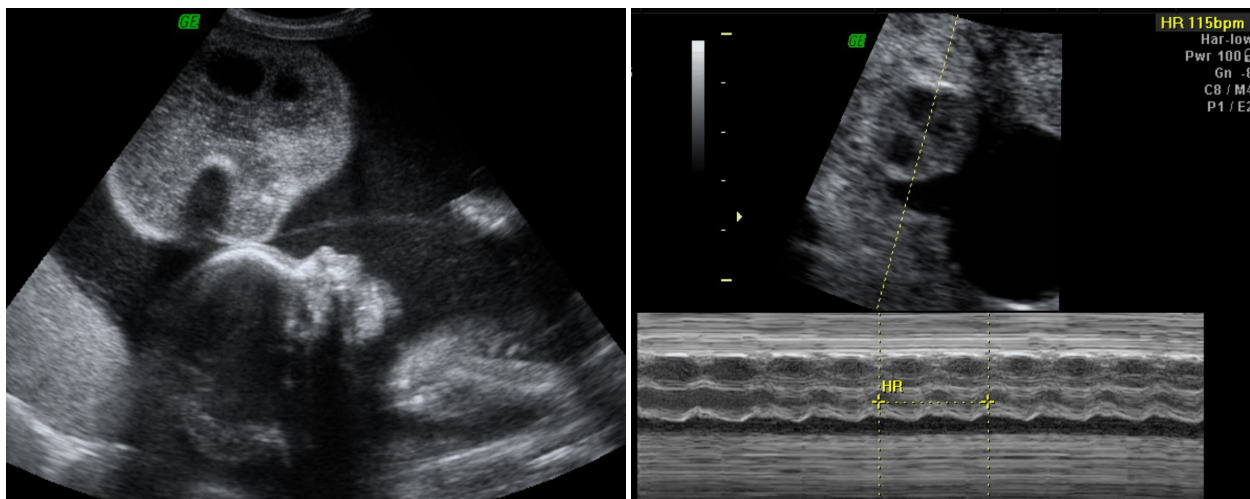


Figure 2 – The echographic aspect of the amniotic membrane, which separates the receptor fetus (up) from the donor fetus (down).

Figure 3 – The receptor fetus – fetal heart with two chambers and an atrioventricular valve, with obvious activity in the M ultrasound mode, 115 beats per minute.

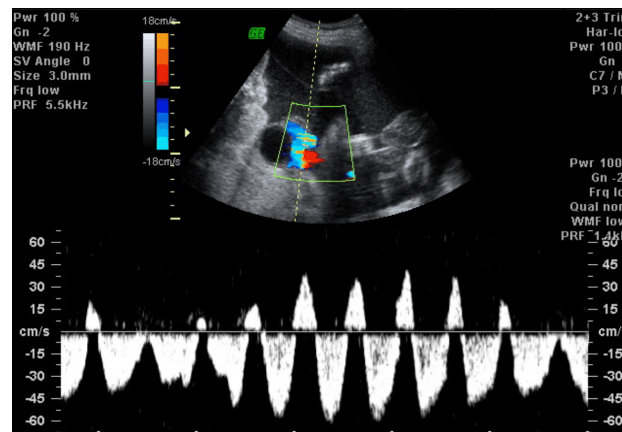


Figure 4 – Doppler ultrasound examination performed on the umbilical artery of the receptor fetus with the presence of the reverse flow.



Figure 5 – The receptor fetus right after the extraction through C-section.

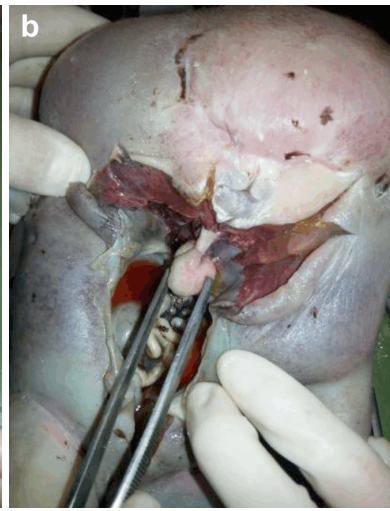
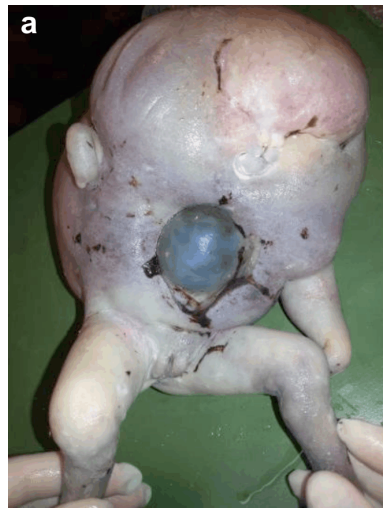


Figure 6 – (a and b) The receptor fetus of the TRAP sequence: in the left picture the abdominal wall defect can be observed and in the right picture, the heart with a unique vessel is visible.



Figure 7 – The placenta, the fetal part, with the vascular anastomosis between the two umbilical arteries.

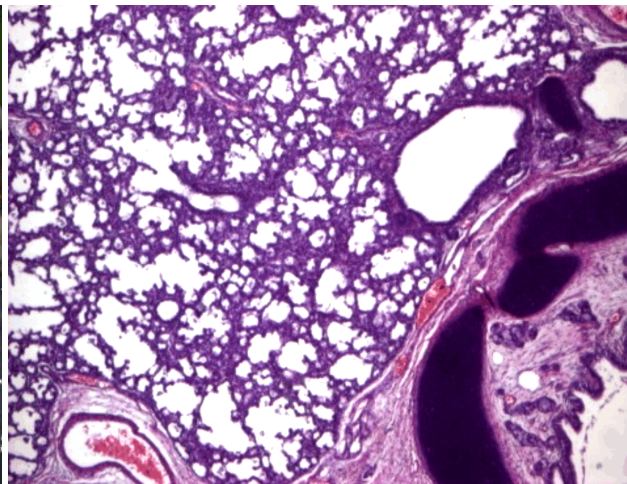


Figure 8 – Immature structure of pulmonary parenchyma (left lung): the irregular air spaces formed predominantly by terminal bronchiole-like structures and clusters of sacs, coated by cubic epithelium. The capillary vessels are present in the surrounding mesenchyme (HE staining, ×100).

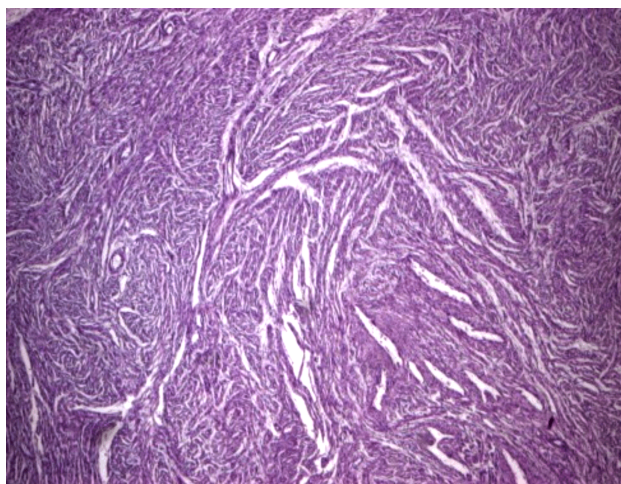


Figure 9 – Ventricular myocardial tissue with striated muscle fibers of various sizes, which show a random arrangement in the vascularized stroma (HE staining, ×100).

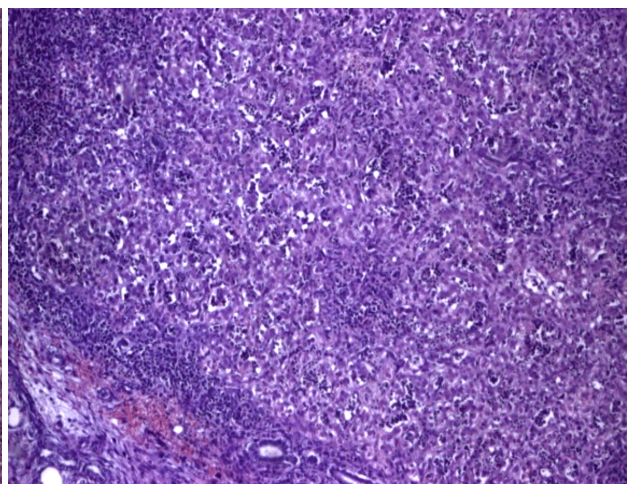


Figure 10 – Immature renal tissue, characterized by islands of mesenchyme within the renal parenchyma (HE staining, ×100).

Discussion

The classification of the TRAP sequence underwent different changes during the time. Therefore, initially, the malformed fetus (the “perfused” twin) was considered acardiac. At the beginning, there were described two groups of acardic twinning: hemicardius (imperfectly formed heart) and holoacardius (absence of the heart), similar classification which was also proposed by Malone & D’Alton [12]. According to this classification, our case can be included in the hemicardius form. According to the Bianchi *et al.* [13] classification in five groups of the TRAP syndrome, our case can be included in acardius myelocephalus because he have a rudiment of head, relative development of the limbs but in contrast of that form, our case had a rudimentary heart. Lachman *et al.* [14] considered that acardius acephalus represent 60–75% of the cases. Guimaraes *et al.* [15], referring to an magnetic resonance imaging (MRI) study, conducted on 35 pregnancies with TRAP sequence, observed that from total evaluated cases 51% were acephalous, 40% were anencephalic (40%), 9% amorphous and none achromous.

Weisz *et al.* described two theories [2] in the pathogenesis of the TRAP sequence: the first – TRAP sequence is a defect in the embryogenesis of the fetal heart and the second, in which TRAP sequence is a vascular primary abnormality with arterial-arterial or venous-venous anastomosis, which leads to premature hypoxia with the lack of organ development, including the heart. Malone & D’Alton [16] emphasized that the perfusion of the “perfused twin” is asymmetric with a relative hypoperfusion of the upper part of the body, leading to significant structural abnormalities.

The presence of the myocardial cells on the pathological samples in the fetuses, which are considered acardial, might support the second theory. In our case, the existence of a bicameral heart, which contains all the three layers, supports the same theory. The natural history of the TRAP sequence may be different from patient to patient [9].

There are at least three known mechanisms by which the acardiac twin can threaten the well-being of the pump twin. Firstly, the parasitic mass produces a systemic shunt, which can increase the cardiovascular demands on the pump twin, leading to congestive heart failure and polyhydramnios. Secondly, continuous growth of the acardiac twin leads to a considerable increase of the intrauterine volume. Thirdly, the blood from the pump twin is deoxygenated, and will be further deoxygenated as it passes through the acardiac mass. This so-called ‘double-used’ blood will then travel back to the pump twin through the vein-to-vein anastomosis, thus reducing the oxygenated supply of blood to the pump twin, which may lead to chronic hypoxia and growth restriction of the pump twin [1]. These changes explain the anemia and cardiac failure to the pumping twin, as it was in our donor twin too. More, our pumping twin died 10 days later due to the anemia and its complications and cardiac failure.

From a morphopathological point of view, the term ‘acardia’ is most frequently used to describe exactly this type of defect. However, the term is rather inappropriate for the following reasons: there is not always a complete absence of the heart and there are often many organs

and structures other than the heart missing [17]. The phenotype of the donor fetus includes anencephaly, holoprosencephaly, absent limbs, absent lungs or heart, intestinal atresia, abdominal wall defects, and absent liver, spleen, or kidneys [5]. The receptor fetus was found as acardiac in 86% of the cases, 100% had an abnormal or absent thorax, 100% had abnormalities of the abdominal organs, 43% had an absence of the superior limbs or abnormal superior limbs (51%), while the presence of the inferior abnormal limbs was reported in 83% of the cases [12]. Similarly, only five (8%) donor fetuses out of 60 TRAP sequences were described as having a partial cardiac structure (pseudoacardiacs) [18]. Neuropathological examination clearly demonstrated two types of changes: a stop in the development of the brain at the prosencephalic stage (holoprosencephaly) and hypoxic damage to the holospheric brain mantle with cystic change (hydranencephaly) [19]. A case in which an abdominal wall defect was found in both fetuses has also been reported [20]. Approximately a third of the fetuses with acardia have an abnormal karyotype and around 9% of the ‘pump twins’ have trisomy [4, 21]. More than one finding has reported the existence of a single umbilical artery (66%) [21].

In our case, the receptor fetus had all the anomalies described above, with the particularity of the simultaneous existence of a rudimentary heart (hypoplastic, univentricular, uniauricular heart, with a present aorta from which the left pulmonary artery emerges, right pulmonary artery agenesis, inferior vena cava agenesis) and a skull with holoprosencephaly, anophthalmia, cystic hygroma. Our case had also other associated malformations like right lung agenesis, left lung hypoplasia, hepatic agenesis, diffuse subcutaneous edema, present pancreas and kidneys, absent urinary bladder. In comparison with the data from literature, the association with a donor fetus, which lacks abnormalities, is very rare.

The first ultrasound description belongs to Lehr & DiRe [22]. The diagnosis is often established after 20 weeks of gestation, as it was seen in our case – at 26 weeks of gestation. An abnormal heart, which had a single chamber, has also been described in the literature [2, 23]. The diagnosis is the prerogative examination of the ultrasound description and confirmed by pathological examination.

The ‘pump twin’ develops polyhydramnios, together with signs of cardiac failure: cardiomegaly, tricuspid regurgitation, pericardial fluid. Doppler ultrasound of the umbilical cords has demonstrated that the direction of flow in the umbilical artery and vein is reversed in the acardiac twin [16]. This sign was firstly described by Pretorius *et al.* at 10–12 weeks of gestation [24] and also by other authors [23, 25], is constant in all cases [10] and was present in our case too. The differential diagnosis should be considered: intrauterine fetal demise of one fetus and anencephaly [16, 18, 26]. Other differential diagnoses, which are less common, include intra-amniotic or placental tumors. However, these conditions can be easily distinguished from acardiac twins by the lack of spinal development and the umbilical cord attachment [1]. According to the evolution, twin reversed arterial perfusion implies a high mortality rate between the first

and early second trimester of pregnancy [27]. The overall perinatal mortality ranged between 35% and 55%, primarily associated with pre-maturity [4, 28]. An acardiac pump twin weight ratio of over 50% is associated with the development of polyhydramnios and preterm labor [21]. Our case also was with polyhydramnios and also premature born. Poor prognostic factors are: a rapidly growing hydropic and large acardiac twin, along with a pump twin, which has signs of cardiac failure and blood flow velocity waveforms, which indicate low resistance in the umbilical artery of the acardiac twin [18].

Weisz *et al.* [2] have proposed a tailored management, which implies that the decision for conservative vs. invasive treatment should be based on ultrasound findings. Criteria for umbilical cord occlusion included: abdominal circumference of the reversed arterial perfusion fetus that was more than or equal to the one of the pump twin, polyhydramnios, abnormal Doppler studies, hydrops of the pump twin or monoamniotic twins [2, 29].

Regarding the invasive treatment, coagulation of the umbilical cord vessels of the acardiac twin was described, with the help of: fetoscopic laser coagulation [30], radiofrequency ablation [3, 31, 32], intrafetal alcohol ablation of the acardiac twin and amniodrainage [33], interstitial laser therapy – feasible from the 13th week of gestation [34], high-intensity focused ultrasound with exposure from outside the maternal abdomen [35]. If a patient presents in the later part of pregnancy with polyhydramnios and evidence of heart failure in the pump twin, alternative methods like caesarian section can be considered [30].

✉ Conclusions

The existence of a rudimentary heart and a vascular anastomosis between the two umbilical cords supports the development of TRAP sequence. The early diagnosis of this pathology, the observation of the pregnancy with the help of weekly ultrasounds and the intrauterine interventions can increase the survival chances of the donor fetus from the TRAP sequence. Anemia and cardiac complications which can lead to cardiac failure, appear early during pregnancy and can be the death cause of the pumping twin. Our case with TRAP was a particular one because it's rarely association of the simultaneous existence of a rudimentary malformed heart and brain and also associated with other abnormalities (abdominal wall abnormality, absent bladder with present kidneys and absence of the lungs), malformations incompatible with life. The ultrasound examination established the diagnosis of the syndrome with high accuracy.

Conflict of interests

The authors declare that they have no conflict of interests.

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