Case Report

Dextro-transposition of the great arteries in one twin: case reports and literature review

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Background: Dextro-transposition of the great arteries (D-TGA) is a rare congenital heart disease, as it affects only 0.02–0.05% of live births. It is the second most common cyanotic heart disease following Tetralogy of Fallot. It has a male predominance. Fetal echocardiography is an optimal method for prenatal diagnosis of fetal D-TGA. In twin pregnancies, fetal D-TGA in one twin is very rare, especially in monochorionic-diamniotic twin pregnancies. Herein, we report a case of D-TGA in one twin in two dichorionic-diamniotic twin pregnancies and one monochorionic-diamniotic twin pregnancy from January 2018 to June 2021.

Case Description: One twin with D-TGA was diagnosed by fetal echocardiography in the second trimester, and the co-twin was normal in all three cases. A multidisciplinary team provided extensive counseling regarding the D-TGA twin and the co-twin, and adequate perinatal management was provided. In cases 1, 2, and 3, the mothers underwent cesarean sections at 37 weeks + 2 days, 34 weeks + 5 days, and 36 weeks + 1 day, respectively. In case 1, which involved a female D-TGA neonate with birth weight 2,410 g, an emergent atrial septostomy was performed at 20 h after birth, and the neonate underwent atrial switch operation (ASO) 24 days after birth. In case 2, involving a male D-TGA neonate with a birth weight of 2,380 g, ASO was performed 24 days after birth. In case 3, involving a female D-TGA neonate with birth weight 2,240 g, ASO was performed 19 days after birth and delayed sternal closure was performed 4 days later. All six infants showed normal development during follow-up.

Conclusions: Early antenatal diagnosis of D-TGA in one fetus of a twin pregnancy is significantly important. A multidisciplinary team should carry individual evaluation and integrated management of the D-TGA twin and co-twin during the pregnancy and perinatal period. After birth, delayed ductus arteriosus closure in the D-TGA twins should be performed when necessary and individualized timings for arterial switch operation should be considered.

Keywords: Dextro-transposition of the great arteries; atrial switch operation; monochorionic-diamniotic twin pregnancy; dichorionic diamniotic twin pregnancy; one twin

Submitted Dec 03, 2021. Accepted for publication Feb 25, 2022.
doi: 10.21037/tp-21-569
View this article at: https://dx.doi.org/10.21037/tp-21-569

Introduction

Dextro-transposition of the great arteries (D-TGA) has been reported to account to 4% of all CHD (congenital heart disease) cases (1) and is defined as a swap between the location of the pulmonary artery and the aorta, with the relationship between the atrium and ventricle remaining unchanged (2). The prevalence of D-TGA is 0.02–0.05% of live births (2-6), and perioperative mortality is about 4% (7,8). Arterial switch operation (ASO) is the common surgical procedure used to treat D-TGA, with a low operation mortality of 2–3% (5,9), long-term benefits (9), and a high survival rate (5,10). According to whether D-TGA is isolated or associated with other congenital heart defects, it can be classified as simple or complex (4). It can also be classified as planned D-TGA which only need prostaglandin E1 for later surgery and emergent D-TGA which must be intervened immediately after birth (11,12). We report three cases of one twin with D-TGA, describing how timely intervention allowed the survival of both twins. Further, we used a list of keywords including "D-TGA," "dextro-transposition of the great arteries," "twin pregnancy," and "multiple pregnancy" to perform an extensive search and conduct a literature review in English and Chinese. We present the following cases in accordance with the CARE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-21-569/rc).

Case presentation

All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patients or legal guardians for publication of this article and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Case 1

A 28-year-old woman, gravida 3 para 0, underwent *in vitro* fertilization and embryo transfer (IVF-ET); two embryos were transferred to the uterus. Ultrasound examination in the first trimester revealed dichorionic diamniotic twin pregnancy. Serological analysis revealed negative results for human immunodeficiency virus (HIV) and the venereal disease research laboratory (VDRL) test. The tests also revealed hepatitis B surface antigen (HBsAg), hepatitis B e antibody, and hepatitis B core antibody positivity for 11 years. The couple had no reported history of medication, substance abuse, or family history of congenital anomalies. Noninvasive prenatal testing (NIPT) was performed at 16 gestational weeks, and no abnormality was reported. At 22 gestational weeks, the woman was transferred to our hospital because one twin had D-TGA. D-TGA was confirmed in Twin A using fetal echocardiography (*Figure 1*). Amniocentesis of both twins was performed and revealed that twin A had chromosome micro-repetition in one specimen (arr[GRCH 37]*q21.32 (92412413-93274528)*3 862 kb). The couple was extensively counseled by the multidisciplinary team (including fetal medicine doctors, obstetricians, pediatric cardiologists, heart surgeons, genetic doctors, imaging doctors, etc.). The woman was followed up closely with fetal ultrasonography and doppler and fetal echocardiography.

At 37 weeks + 2 days, due to onset of labor, a cesarean section was performed. The healthy male co-twin (twin B) weighed 2,600 g, with Apgar scores of 10 and 10 at the first and fifth minute, respectively. The female twin with D-TGA (twin A) weighed 2,410 g, with Apgar scores of 9 and 9 at the first and fifth minute, respectively. Twin A was transferred to the neonatal intensive care unit (NICU) and prostaglandin E1 was administered for twin A after echocardiography confirmed foramen ovale restriction. Twin A suffered from low peripheral oxygen saturation (80%) and cyanosis, which was sustained for 20 hours after birth. Neonatal echocardiography performed in the pediatric intensive care unit showed congenital heart disease: dextro-transposition of great arteries, patent ductus arteriosus and foramen ovale, and an abnormal origin of the coronary artery with normal systolic function of the left ventricle. Because of foramen ovale restriction, twin A underwent emergent atrial septostomy via the umbilical vein. Two days later, the neonate was hemodynamically stable and had normal peripheral oxygen saturation levels (95%). At 24 days old, twin A underwent arterial switch operation (ASO), atrial septal defect repair, arterial catheter ligation, and temporary pacing wire implantation under cardiopulmonary bypass. The neonate was discharged 12 days after the switch surgery. Both babies were followed up. To date, both babies are one year nine months old and are exhibiting normal development.

Case 2

A 32-year-old woman, gravida 2 para 1, spontaneously

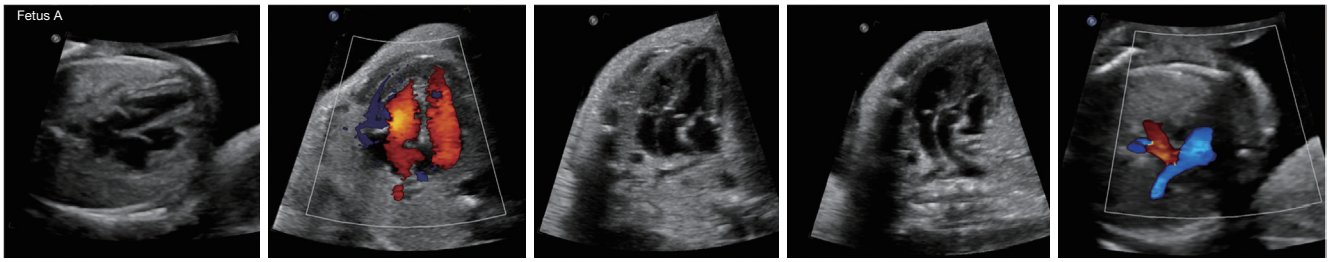

Figure 1 Fetal echocardiography images of twin A with dextro-transposition of the great arteries (case 1).

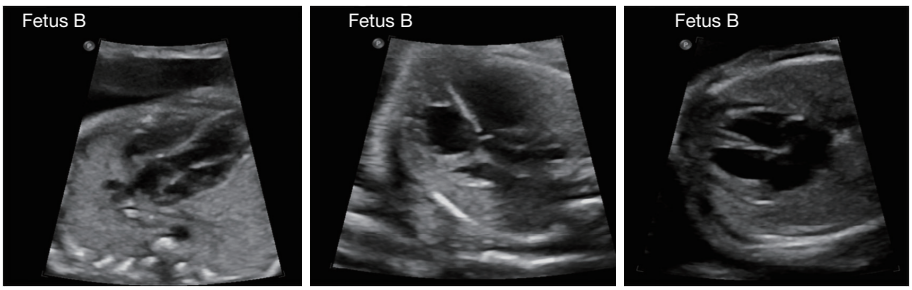

Figure 2 Fetal echocardiography images twin B with dextro-transposition of the great arteries (case 2).

conceived. Ultrasound examination at 9 weeks' gestation confirmed a monochorionic-diamniotic twin pregnancy. She had undergone transverse lower segment cesarean section for a singleton pregnancy 5 years earlier. Serological analysis revealed negative results for HIV, VDRL, and HBsAg, and the patient did not have diabetes mellitus. The pregnant woman and her partner reported no history of medication, substance abuse, or family history of congenital anomalies. At 25 gestational weeks, the woman was transferred to our hospital because of suspected D-TGA in one twin. The NIPT result showed no abnormality. Twin B was confirmed as having D-TGA by fetal echocardiography at our hospital (*Figure 2*). The pregnant woman and her partner were counseled extensively by the multidisciplinary team (including fetal medicine doctors, obstetricians, pediatric cardiologists, heart surgeons, genetic doctors, imaging doctors, etc.), and they refused amniocentesis for both twins. The woman was followed up closely with fetal ultrasonography and doppler and fetal echocardiography.

At 34 weeks + 5 days, the woman underwent emergent cesarean section as she went into labor. The healthy male co-twin (twin A) weighed 2,060 g, with Apgar scores of 10 and 10 at the first and fifth minute, respectively. The male twin with D-TGA (twin B) weighed 2,380 g, with Apgar scores of 9 and 9 at the first and fifth minute, respectively. Both neonates were transferred to the neonatal department. Twin A was discharged after 5 days. At 20 days of age, twin B was transferred to the Department of Cardiac Surgery. After 4 days of preoperative preparations, twin B underwent ASO, atrial septal defect repair, arterial catheter ligation, and temporary pacing wire implantation under cardiopulmonary bypass. Delayed sternal closure was performed 4 days after the operation. The neonate was discharged 9 days after sternal closure. Both babies were followed up. To date, both babies are one year eight months old and are exhibiting normal development.

Case 3

A 31-year-old woman, gravida 3 para 0, underwent IVF-ET; two embryos were transferred to the uterus. Aspirin was prescribed to the patient (50 mg qd) by the local hospital following IVF-ET. Ultrasound examination in the first trimester revealed a dichorionic-diamniotic twin pregnancy. Serological analysis revealed negative results for HIV, VDRL, and HBsAg, and she had diabetes mellitus. The couple had no reported history of medication, substance abuse, or family history of any congenital anomaly. NIPT was performed at 15 + 5 gestational weeks, and no abnormality was documented. At 23 gestational weeks,

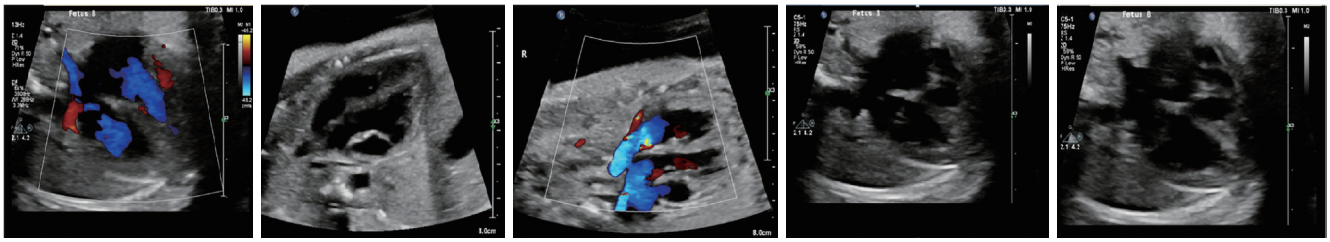

Figure 3 Fetal echocardiography images of twin B with dextro-transposition of the great arteries (case 3).

the woman was transferred to our hospital as one twin was suspected of having D-TGA. Fetal echocardiography at our hospital confirmed D-TGA in Twin B (*Figure 3*). The pregnant woman and her partner were extensively counseled by the multidisciplinary team (including fetal medicine doctors, obstetricians, pediatric cardiologists, heart surgeons, genetic doctors, imaging doctors, etc.), and the woman was closely monitored with fetal ultrasonography and doppler and fetal echocardiography.

At 36 weeks + 1 day, cesarean section was performed due to onset of labor. The healthy female co-twin (twin A) weighed 2,400 g, with Apgar scores of 8 and 9 at the first and fifth minute, respectively. The female twin with D-TGA (twin B) weighed 2240 g, with Apgar scores of 10 and 10 at the first and fifth minute, respectively. Cyanosis was observed in twin B, which sustained for 31 minutes after birth. Prostaglandin E1 was administered after she was transferred to the NICU. Neonatal echocardiography performed in the NICU showed congenital heart disease: dextro-transposition of the great arteries, patent ductus arteriosus and foramen ovale, and normal systolic function of the LV. Chest radiography showed neonatal respiratory distress and pneumonitis. Because of this condition, noninvasive ventilation was performed. The neonate's peripheral oxygen saturation was 85–90% 16 days later, and she was transferred to the Department of Cardiovascular Surgery with intubation. At 19 days old, twin B underwent arterial switch operation (ASO), foramen ovale closure, arterial catheter ligation, and temporary pacing wire implantation under cardiopulmonary bypass. Nine hours after the surgery, chest cardiac compression and repeated epinephrine (i.v.) injections were administered because of a gradual drop in the neonate's heart rhythm. Delayed sternal closure was performed 4 days later. The neonate was transferred to an NICU with intubation 14 days after the surgery and discharged 51 days after the switch surgery. Both babies were followed up. To date, both babies are 8 months old and show normal development.

Discussion

Fetal D-TGA can be classified as planned and emergent, the former only need prostaglandin E1 for later surgery while the later must be intervened immediately after birth (11,12). Fetal ultrasound is the first-line procedure that indicates D-TGA (13). Its prenatal use can reduce mortality and morbidity because the findings can alert doctors to implement emergent neonatal management strategies or interventions such as balloon atrial septostomy, and further, the outcome and long-term neurocognitive function can also be improved (7,13,14).

The D-TGA fetus can tolerate this kind of abnormality because of the well-designed fetal cardiovascular system. Placental circulation between maternal and fetal systems, shunts of the foramen ovale, and ductus arteriosus and ductus venous guarantees adequate oxygen supply in utero, even in a stressful state. However, hypoxemia and cyanosis may develop once the neonatal circulation begins because of impaired physiologic shunts (7). In case 2, the D-TGA fetus with intact ventricular septum developed hypoxemia and cyanosis because of a closed foramen ovale, and an emergent atrial septostomy was performed to alleviate her symptoms; in case 3, cyanosis occurred in the D-TGA fetus after birth and was sustained for more than half an hour, although complicated with patent foramen ovale. However, the incidence of restrictive foramen ovale in D-TGA is about 38–50% (15,16), and its prenatal detection is still challenging (7). From these two cases, we hypothesize that gestational age at birth may affect peripheral oxygen saturation of the D-TGA neonate.

Chromosomal abnormalities found by chromosomal microarray in D-TGA-associated fetuses have been reported earlier (1,17-19). Lee *et al.* (20) suggested chromosomal microarray analysis as an effective tool to

detect chromosomal copy number variation in fetuses with D-TGA and to improve prenatal counseling, postnatal management, and neurodevelopmental outcomes. Skoric-Milosavljevic *et al.* (21) identified a susceptibility locus at 3p14.3, which is known for its important role in cardiac development. Of note, there exist suspect that D-TGA is polygenic inheritance (22,23). In this study, amniocentesis in case 1 revealed chromosome micro-repetition (arr[GRCH 37]*q21.32(92412413-93274528)*3 862 kb) in the D-TGA twin, whereas the co-twin showed no such aberration. Regrettably, the parents refused amniocentesis in case 2 and case 3. Therefore, we believe that chromosomal microarray should be considered in our further research.

In a D-TGA fetus, oxygenated blood is directed to the pulmonary circulation, whereas the blood supplied to the brain is mainly deoxygenated blood returned from the vena cava (24,25). Studies have revealed impaired fetal brain metabolism due to reduced oxygen supply, further causing fetal brain dysmaturation (24,26). Zeng *et al.* (25) prospectively evaluated the volume of intracranial structures in fetuses with congenital heart disease by three-dimensional ultrasound and showed a maximum reduction of the frontal lobe volume after 28 gestational weeks and impaired neuroimaging in 34% of TGA cases. Recently, a study found an increase in the width and length of the cavum septi pellucidi in D-TGA fetuses, indicating that the frontal lobe can be protected from hypoxemia because of vasodilation in the anterior cerebral artery (6). In addition, MCA-PI (pulsatility index of the middle cerebral artery) also decreases in TGA fetuses ($P<0.05$) because of an intrauterine compensatory "brain sparing" response (25). Until now, few studies have reported fetal brain impairment wherein one twin was diagnosed with D-TGA, whereas the other twin was normal, especially in monochorionic twin pregnancies with the placental vascular anastomoses between the two fetuses. In this study, although there was one case with MCDA twin pregnancy, we did not observe similar results as published earlier, and the MCA-PI was not abnormal in the D-TGA twin or the co-twin in all three reported cases.

Arterial switch operation (ASO) is a prevailing surgery procedure for D-TGA, with a low operation mortality rate of 2–3% (5,9) and long-term benefits (9). The 10-year survival rate, following ASO, is 88–97% (5), the 20-year survival rate is nearly 90% (10), and 82% of ASOs require no further operations (5). However, some post-operation complications can occur, including frequently reported neurodevelopment lesions causing reduced performance in tasks assessing attention, visual-spatial skills, and executive functions, as well as anxiety disorders (5). Some large cohort trials have also shown an increased risk of neurodevelopmental delay in patients with TGA (27). Therefore, when symptoms of neurodevelopmental impairment occur in ASO cases, it is difficult to determine whether it results from TGA or post-ASO-operation complications. Further study is needed to confirm this perinatal management and outcomes of one twin with D-TGA. We found 11 cases of one twin with D-TGA. Detailed information is shown in *Table 1*. The prognosis of isolated D-TGA is promising with appropriate management. Analyzing of these cases (3,28-37) gave insight to us on the intervention of D-TGA cases.

We report D-TGA in one twin in two dichorionic twin pregnancies and one monochorionic twin pregnancy. Both the maternal and fetal conditions were dynamically monitored and evaluated by a multidisciplinary team during the pregnancy. In addition, ASO was performed in three D-TGA fetuses after birth, and one patient underwent emergent atrial septostomy before ASO. The mothers and infants were in good health on follow-up, and long-term follow-up is underway.

Conclusions

In conclusion, D-TGA in one fetus of twin pregnancy is very rare, especially in monochorionic twin pregnancies. Therefore, early antenatal diagnosis is significantly important. Once the D-TGA is diagnosed, clinicians should be aware of the associated maternal and fetal complications. Full-term birth may have more benefits. Individualized evaluation and integrated management of the D-TGA twin and co-twin during pregnancy and the perinatal period should be carried out by the multidisciplinary team. After birth, delayed ductus arteriosus closure in the twin with D-TGA should be performed when necessary. Individualized timing of ASO in the twin with D-TGA after

Table 1 Reported cases of transposition of the great arteries in one twin

Study ID	Type of twin	Diagnosis age (wks)	Delivery age (wks)	Delivery method	TGA twin						Non-TGA twin	
					Other cardiac malformation	Extracardiac malformation	Complications	Birth weight	Surgery therapy	Outcome	Birth weight (g)	Outcome
De Ugarte DA 2002 (28)	Acardiac, acephalic, parasitic conjoined twins	After birth	38	CS	Aortic coarctation, PDA, PFO, and 2 VSDs	Large omphalocele	/	Live birth weighing 3,000 g in total	DOL 4, cardiac catheterization and Rashkind balloon atrial septostomy; DOL 8, Exploratory laparotomy; DOL 13, segment of small bowel with Meckel's diverticulum removed, and an end ileostomy performed; DOL 26, a left thoracotomy for repair of the aortic coarctation, pulmonary artery banding, ligation of the PDA, and plication of a left flail diaphragm performed; DOL 75, arterial switch procedure and repair of ASDs and VSDs, and an end ileostomy was performed	DOL 117, discharged home on diuretics, digoxin, and aspirin	NS	Acardiac, acephalic, parasitic conjoined twin
Üstüner I 2005 (29)	MCMA acardiac acephalic twin	27	NS	VD	NS	NS	TRAPS (pump twin)	620 g	No	TOP	390 g (including the placenta)	Acardius acephalus mass
Ezra Y 2005 (30)	MA twin	NS	NS	NS	NS	NS	NS	NS	NS	Liveborn	NS	Liveborn
Tongsong T 2005 (31)	Thoraco-omphalopagus twins	18	NS	VD	Shared heart with another conjoined twin	Thoraco-omphalopagus twins, shared upper liver and anterior chest wall, one umbilical cord which contained four vessels	NS	460 g in total conjoined twins	NS	TOP	/	TOP
Steggerda S 2006 (32)	MCDA twin	18	30	CS	Ventricular septal defect, double outlet right ventricle with myocardial hypertrophy, and a small pulmonary artery	NS	TTTS (recipient twin)	Live birth weighing 800 g	No surgery therapy	Died 49 days after birth due to pulmonary and cardiac conditions worsen	93 g (donor twin)	Umbilical cord coagulation at 18 wks
Kaneko Y 2007 (33)	Monozygotic twin	After birth	31	NS	NS	NS	Cyanotic	1,146 g	Arterial switch operation performed at age of 14 days	Extubated at age 28 days and discharged at age 109 days with. normal left ventricular function, a widely patent neoaorta–coronary artery tunnel, and mild neopulmonary regurgitation	NS	NS
Chen G 2012 (34)	Thoraco-omphalopagus conjoined twins	NS	36	CS	NS	Thoraco-omphalopagus conjoined twins	Sepsis, NEC	5,985 g in total conjoined twins	Arterial switch and complete repair of her cardiac defect at 25 days of life	Extubated on day 10 and discharged 20 days after cardiac surgery	NS	On the eighth day of life, separation surgery performed and ventilation performed for 10 days after separation; an uncomplicated recovery
Bravo-Valenzuela NJ 2017 (35)	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Richtsfeld M 2017 (36)	Thoraco-omphalopagus twins	Before delivery	34	CS	Tricuspid Atresia, atrial septal defect, ventricular septal defect	Thoraco-omphalopagus twin	NS	NS	Atrial septostomy at 3 months of age	Extubated in the catheterization laboratory and transported to the ICU	NS	Extubated in the catheterization laboratory and transported to the ICU
Ravi P 2018 (3)	MCMA	NS	NS	NS	NS	NS	NS	NS	NS	Liveborn	NS	NS
Haranal M 2020 (37)	Thoraco-omphalophagus conjoined twins	NS	NS	NS	Non	Thoraco-omphalophagus twins, right lung hypoplasia	Non	NS	DOL 1, emergent BAS; DOL 15, surgical separation; DOL 25, PDA stented; 3 months of age, arterial switch operation	Extubated on postoperative day 20, with good biventricular function, mild tricuspid regurgitation (TR), no right or left ventricular outflow tract obstruction, good flow in the branch pulmonary arteries on discharge; be doing well on subsequent follow-up visits	NS	DOL 15, surgical separation
Our cases	DCDA	22	37+2	CS	Non	Non	Non	2,410 g	Emergent atrial septostomy 20 hours after birth; ASO at 24 days of life	Normal development	2,600 g	Normal development
	MCDA	25	34+5	CS	Atrial septal defect	Non	Non	2,380 g	Atrial septal defect repair and ASO at 24 days of life	Normal development	2,060 g	Normal development
	DCDA	23	36+1	CS	PDA, foramen ovale	Non	Non	2,240 g	Foramen ovale closure and ASO at 19 days of life	Normal development	2,400 g	Normal development

wks, weeks; TGA, transportation of great arteries; CS, cesarean section; PDA, patent ductus arteriosus; PFO, patent foramen ovale; VSD, ventricular septal defect; DOL, day of life; NS, not specified; MCMA, monochorionic monoamniotic; VD, vaginal delivery; TOP, termination of pregnancy; MA, monoamniotic; MCDA, monochorionic diamniotic; NEC, neonatal necrotizing enterocolitis; DCDA, dichorionic diamniotic; ASO, arterial switch operation.

birth should be considered, and emergent operation, such as atrial septostomy, should be performed when needed.

Acknowledgments

We are grateful to the doctors and staff involved in this work. We are also grateful to the doctors and staff of the Department of Cardiac Surgery in West China hospital.
Funding: This study was supported by the Academic and Technical Leader's Foundation of Sichuan Province (No. 2017-919-25).

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-21-569/rc

Peer Review File: Available at https://tp.amegroups.com/article/view/10.21037/tp-21-569/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-21-569/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patients or legal guardians. A copy of the written consent is available for review by the editorial office of this journal.

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Cite this article as: Hu Q, Deng C, Zhu Q, Yang X, Liu H, Liao H, Wang X, Yu H. Dextro-transposition of the great arteries in one twin: case reports and literature review. Transl Pediatr 2022;11(4):601-609. doi: 10.21037/tp-21-569