American Journal of Pediatrics
2023; 9(1): 1-4
http://www.sciencepublishinggroup.com/j/ajp
doi: 10.11648/j.ajp.20230901.11
ISSN: 2472-0887 (Print); ISSN: 2472-0909 (Online)

Trisomy 18: Anti-Congestive Drug Treatment Combined with Transcatheter Occlusion of an Arterial Duct and Misaligned Perimembranous VSD

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To cite this article:

Tim Schubert, Anoosh Esmaeili, Dietmar Schranz. Trisomy 18: Anti-congestive Drug Treatment Combined with Transcatheter Occlusion of an Arterial Duct and Misaligned Perimembranous VSD. *American Journal of Pediatrics*. Vol. 9, No. 1, 2022, pp. 1-4.
doi: 10.11648/j.ajp.20230901.11

Received: November 22, 2022; **Accepted**: December 12, 2022; **Published**: January 17, 2023

Abstract: *Background* Trisomy 18 syndrome, the second most common autosomal numerical chromosomal disorder, is associated with multiple-organ abnormalities. Cardiovascular malformations are just one of those affecting prenatal and postnatal life expectancy. In general, the type and scope of treatment are still controversial and are handled very differently. Palliative care usually focuses on improving quality of life or life-threatening conditions. *Objective* Based on parental treatment preferences for their child, we report the anticongestive drug treatment and consecutive transcatheter therapy of cardiac shunt lesions in a girl with trisomy 18 who was born small-for-date. *Methods* Anticongestive drug treatment was switched form diuretic-directed drug treatment to our standard care for chronic heart failure in infants, which consists of a ß1-specific beta-blocker (bisoprolol) in combination with an ACE-inhibitor (lisinopril) and a low-dose mineralocorticoid-blocker (spironolactone). In addition, the strategy and technique of semi-invasive transcatheter treatment of significant cardiovascular shunt lesions is reported. At 3 months of age and weighing 2.4kg, a significant arterial duct was first occluded percutaneously with an MVP-5Q device, followed by transcatheter closure of a slightly misaligned perimembranous VSD six weeks later. Both interventions were performed on a spontaneously breathing only sedated baby. *Results* The device strategy for treating the hemodynamically significant cardiovascular shunt lesions was technically feasible and effective in combination with medication. However, the medium- or long-term outcome cannot be defined due to the limitations caused by the syndrome. *Conclusion* As part of a medical risk-benefit assessment, the parents should make the decision as to whether their child should be treated or not; the responsible physicians have individually to offer the best treatment option.

Keywords: Trisomy 18, Transcatheter Treatment, Patent Arterial Duct, Ventricular Septal Defect, Congestive Heart Failure, Case Report

1. Introduction

Trisomy 18 is the second most common autosomal trisomy with incidences reported from 1/3.000 to 1/8.000 with an average lifespan of 3-14 days. Less than 10% survive one year [1, 2]. Pathognomonic morphological criteria were first described in 1960 [3]. Congenital cardiac malformations are commonly found in patients with trisomy 18. They are considered a cause of death when associated with heart failure [4]. Ventricular septal defect (VSD) is generally the most common cardiac defect associated with active pulmonary congestion, particularly when coexisting with a significant arterial duct (PDA) [5]. Malalignment ventricular septal defect means that there is malalignment between the apical and outlet parts of the ventricular septum or some present degree of overriding of the leaflets of an arterial valve [6]. Despite their prevalence, few cardiac malformations are treated in infants with trisomy 18 [7]. As part of a comprehensive strategy, our report focused on the percutaneous closure of a misaligned perimembranous

ventricular septal defect in a 5-month-old girl previously treated for PDA.

2. Case Presentation

The girl was born small-for-date with a birth weight of 1.9kg. Prenatal diagnostics showed growth retardation, cerebellar hypoplasia and cardiac defects classified prenatally as atrio-ventricular cardiac septal defect (AVSD). Continuous positive airway pressure (CPAP) support was required for the first 3 postnatal days. Due to clinical symptoms, visible malformations and congenital heart defects, the urgent suspicion of Edwards-Syndrome as a free trisomy 18 was confirmed. Due to cardiovascular shunt lesions, progressive congestive heart failure developed while pulmonary vascular resistance (Rp) decreased. Given this history, the baby was referred to our centre for optimizing heart failure therapy and intended PDA closure. At the age of almost 3 months (body weight of 2.4kg), the fetal-type PDA with a minimal diameter of 3mm was closed percutaneously with an MVP-5Q device (MicroVascularPlug, Medtronic®) with a short fluoroscopy time of less than 2 minutes (Figure 1a b). Chronic anti-congestive treatment, based primarily on diuretics, was changed to once per day doses of bisoprolol (0.2mg/kg), lisinopril (0.2mg/kg) and spironolactone (1-2mg/kg). Along with further body and subsequent heart growth, the perimembranous ventricular septal defect also increased in diameter from 4-5 to 6-7mm. Transient respiratory and cerebral disturbances, including apnoea tendencies, required intermittent oxygenation, which in turn led to left-to-right shunt augmentation with consecutive pulmonary congestion. The girl, who was still tube-fed, now weighted 3.6kg. Under stable conditions, there was a systolic murmur of 3/6°, a resting heart rate of about 125/min, a blood pressure 89/48mmHg and pulse-oximetry oxygen saturation above 93%. Transthoracic echocardiography (TTE) showed a significant left-to-right-shunt across a perimembranous VSD that was slightly misaligned with respect to the aortic valve. The PDA was completely closed, left pulmonary artery and descending aorta unobstructed, aortic and pulmonal valves competent. The hypertrophied right ventricle contracted well with mild tricuspid regurgitation. In regard of the congestive heart failure, the intermittent need for oxygenation and a detailed risk-benefit assessment, we decided in favour of percutaneous VSD closure together with the parents who work as an ICU-nurse and a radiologist. Following written informed consent, the baby was again catheterized under analgosedation. Right femoral groin was prepared under aseptic condition and 4Fr Terumo® sheaths were placed in the right femoral artery and vein. Pulmonary to systemic artery diastolic pressure ratio was 0.46 (18 to 39mmHg), superior vena cava oxygen saturation (SO_2) was 68%, and pulmonary trunk SO_2 was 89%, indicating a left-to-right shunt or Qp/Qs suggests of almost 3.7. LV angiography performed through a 4Fr Pigtail catheter did not clearly demonstrates the VSD morphology. After exchanging the catheter for a right 4Fr Judkins right (2.5-JR), the JR was easily advanced through the misaligned VSD in the right ventricle. Therefore, we favoured a retrograde transcatheter approach. A soft-coronary-wire originally placed in the pulmonary artery, was eventually replaced with a 0.035inch guide wire (Figure 2a). The femoral artery was gradually dilated by exchanging a 4Fr for a 6Fr Terumo® sheath, followed by a 5F delivery sheath for placement of a KonarLT-MFO-7-5 Occluder (LifeTech®). With respect to the femoral artery, the marginal long-delivery system was retrogradely advanced through the aortic valve and VSD into the apex of the right ventricle (RV). Then the cccluder was screwed on its left side and the right umbrella opened in almost the middle of the RV cavity (Figure 2b). The conically shaped stent between the two umbrellas was positioned exactly inside the VSD and the left-sided umbrella was finally pushed down towards the LV-apex (Figure 2c). The final angiography and a second post-release echocardiography showed the correctly positioned VSD-occluder with just a trivial shunt through the device (Figure 3a, b). A single dose of 400U heparin was administered periprocedurally, followed by an intravenous infusion of 300U/kg/day. The total fluoroscopy time was 14.49 minutes, the total area dose 364.15µGym². The patient was discharged home on the third day after the intervention. Drug treatment was reduced to bisoprolol and spironolactone; 5mg aspirin once daily was added.

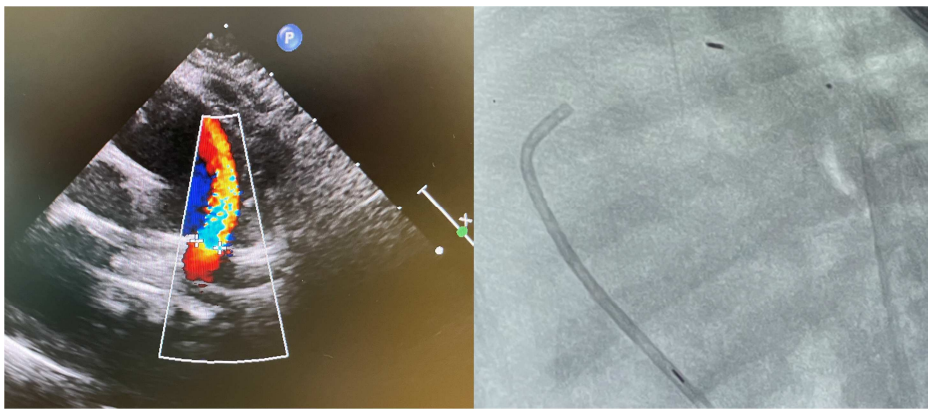

Figure 1. *Shows the echocardiography with color-Doppler tubular of a tubular, fetal-like type left-right shunting arterial duct and the fluoroscopy frame after ductal closure by a MVP-5Q (Medtronic® plug system) in a lateral projection.*

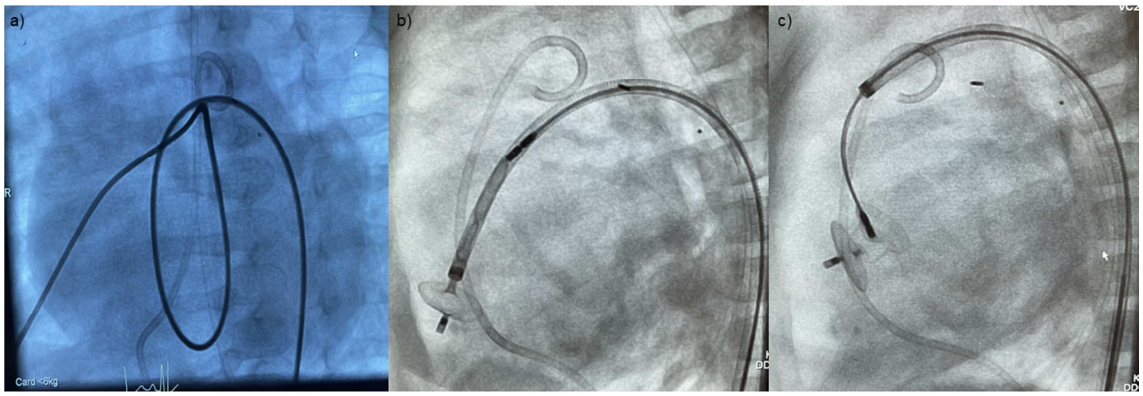

Figure 2. *a). Anterior-posterior fluoroscopy plane demonstrating the ensemble of a 4Fr right Judkins (2.5JR) catheter together with 0.0036" guidewire as the premise to position the delivery system for transcatheter ventricle septum defect closure. b). Lateral 90° fluoroscopy plane shows a retrograde positioned 5Fr delivery system within the right ventricle. The right-sided umbrella of the MFO-device is just expanded.* ***c).*** *Lateral 90° fluoroscopy plane shows the completely expanded, but not released MFO-device within the ventricular septum defect.*

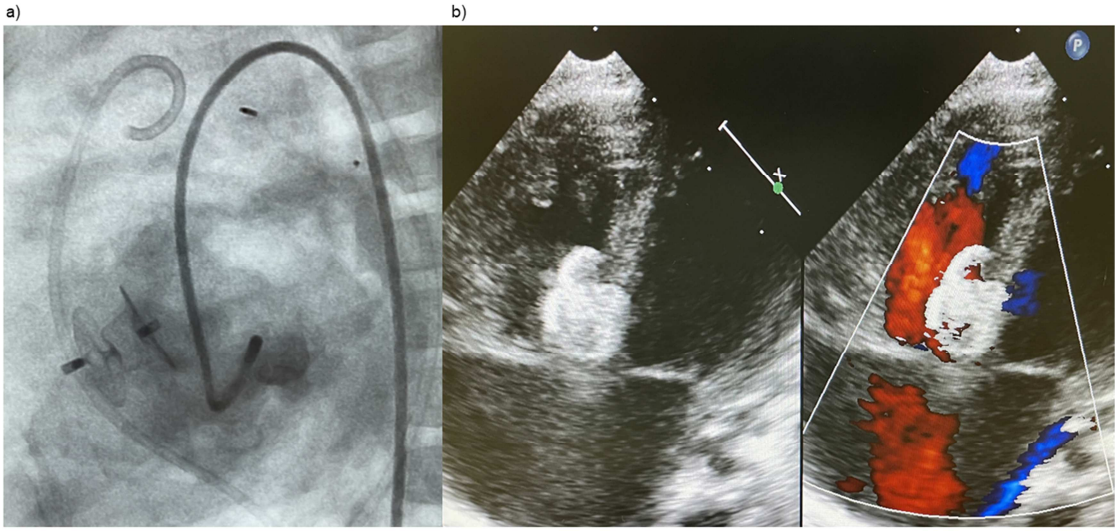

Figure 3. *a). Final angiography is shown in lateral 90° projection; in addition to an MFO-device placed in the VSD, the MVP-device within the arterial duct as well as a second pigtail catheter still in the pulmonary artery are depicted. b). postprocedural echocardiography four chamber view without and with colour confirm the correctly placed Occluder.*

3. Discussion

There is actually no data to compare our case report with. In contrast to small series of corrective surgeries, sequential transcatheter closures of hemodynamically significant PDA and perimembranous VSD in a young infant with Trisomy 18 have not been described to our knowledge.

When it comes to the question of whether we should treat a patient with trisomy 18 or not, the immediate relief of the ventricular workload and the improved general condition should be checked. Based on the advanced device developments and improved catheter technology, PDA closure can technically be offered to almost all patients regardless of age, body weight and ductal size [8, 9]. The MVP-set is almost ideal for duct closure with a tubular, fetal -type morphology [10].

The transcatheter technique for percutaneous closure of ventricular septal defects, in particular that of the perimembranous VSD, was a similar but in regard of the morphology and patient's size not yet completed development [11, 12] However, ventricular septal defects are often an integral part of complex lesions or coexist with other shunt lesions. Correction of congenital shunt lesions is not necessarily curative, especially in connection with genetic syndromes as Trisomy 18 [13]. Given the morphology of some VSDs, surgical repair is the only option. However, when a percutaneous transcatheter procedure is technically possible, one can expect reduced risks in terms of myocardial injury, avoidance of anaesthesia and critical care, shorter hospital stays and recovery time [14]. Some procedural risks we had considered as device-related residual shunt or even tricuspid valve regurgitation, device dislodgement and the increased risk a complete heart block [15]. However, the main concern from the technical point of view was the risk of arterial vessel injury, particularly in context of the marginally sized delivery system given the still low bodyweight. Eventually, the slightly misaligned positioning of the perimembranous VSD facilitated the decision to use the retrograde VSD closure approach.

4. Conclusion

In conclusion, one of the most difficult questions remains whether a child with trisomy 18 should treat at all. Again, this decision was simplified by the parent's medical expertise, including their desire for the preferential transcatheter approach. Overall, the improvement in life expectancy or quality of life in children with trisomy 18, even after cardiovascular correction, remains unclear.

Financial Support

This research received no specific grant from any funding agency, commercial or non-profit sectors.

Ethical Standards

Treatment and case report is performed by written informed consent of the parents and corresponds to the institutional ethical rules.

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