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CASE REPORT

Echocardiographic features in infants with dilated cardiomyopathy treated with reversible pulmonary banding: a preliminary single-centre experience

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ABSTRACT

Reversible pulmonary artery banding (rPAB) was proposed as an innovative therapy for young children with end-stage heart failure due to dilated cardiomyopathy (DCM). We report our early experience with rPAB in 2 infants with DCM and preserved right ventricle (RV) function to evaluate the effectiveness of this treatment. Pre- and postoperative echocardiography included standard evaluation of right (RV) and left (LV) ventricle global systolic function. Moreover, we applied the LV global longitudinal strain for better analysis of LV systolic function. During 15 months of follow-up, clinical and echocardiographic improvement was observed. Our early experience indicates that rPAB may be an effective alternative to heart transplantation or recovery in selected children with DCM.

KEY WORDS:

myocardial strain, dilated cardiomyopathy, reversible pulmonary artery banding, children.

INTRODUCTION

Dilated cardiomyopathy (DCM) is the most common form of paediatric cardiomyopathy, with a reported annual incidence of 0.58–0.78 cases per 100,000 children [1]. Dilated cardiomyopathy is defined as left ventricle (LV) dilatation and LV dysfunction in the absence of abnormal loading conditions or coronary artery abnormalities. Epidemiological studies have reported that most children with DCM present under the age of one year and up to 93% are symptomatic, with features of congestive heart failure (HF) at presentation. The aetiology of DCM is heterogeneous, particularly in the paediatric population, and it includes acquired and inherited causes.

The basic echocardiographic parameters confirming the diagnosis of DCM are left ventricle end diastole diameter (LVEDD) and left ventricle end systole diameter Z-score ≥ 2 (determined as more than 2 standard deviations from the mean value for the population corrected for body surface area [BSA]) and decreased systolic function [2]. Recent literature reports indicate that the left ventricle global longitudinal peak strain (LVGLS) may be useful in diagnosis as well as in predicting outcomes in children with DCM [3]. Reversible pulmonary artery banding (rPAB) is a novel therapeutic strategy proposed in children younger than 3 years of age with end-stage HF due to DCM and preserved right ventricle (RV) function, which improves LV parameters by ventriculo-ventricular interaction. The reversible pulmonary artery banding is performed to obtain a RV pressure equal to 60% of systemic blood pressure, as recommended in the literature [4]. This surgical procedure allows the avoidance or delay of heart

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transplantation (HTx) in paediatric DCM [4, 5]. The aim of our report was to present the predictive value of LVGLS in assessing the efficacy of rPAB in 2 infants with DCM.

MATERIAL AND METHODS

The transthoracic (TTE) and transoesophageal echocardiography were obtained on a Philips Epiq7 (Philips Medical Systems, Bothell, WA). Myocardial strain analysis was performed from 2-dimensional (2-D) imaging using Philips Software. In the described 2 children, we evaluated conventional RV and LV global systolic function parameters and speckle tracking analysis of 2-D left ventricle global longitudinal strain (2-D LVGLS) before and after rPAB. Our patients fulfilled the inclusion criteria for rPAB recommended in the literature [4]: age < 3 years, severe LV systolic dysfunction (EF < 30% calculated by the Simpson method), LVEDD Z-score > 4, preserved RV function, and no efficacy of phar-

macological treatment of HF, including inotropic positive drugs. Congenital heart disease and pathology of the coronary arteries were excluded in both infants. The echocardiographic diagnosis of DCM was confirmed by cardiovascular magnetic resonance imaging. Genetic testing using the next-generation sequencing technique and panel of 57 genes related to the aetiology of DCM was performed in both children. Each patient was also screened for metabolic disorders. Patients were followed prospectively for 15 months. Clinical examination, evaluation of somatic growth and symptoms of HF (Ross classification), and the value of biomarker NT-proBNP were repeatedly performed during the follow-up period. Transthoracic was performed on hospital admission and on bi-monthly visits during follow-up. Cardiac catheterization was performed in case 1. Transoesophageal echocardiography was done during the rPAB procedure to allow tightening of the band until re-shifting of the interventricular septum to the midline position (evaluated

TABLE 1. Echocardiographic measurements in case 1 (M.B.)

TTE	Before rPAB	During procedure of rPAB (TEE)	At discharge	After rPAB 5 mo	After rPAB 11 mo	After rPAB 15 mo
LVDD [mm]	47 ($Z = +8$)	–	48 ($Z = +8.8$)	45 ($Z = +7.6$)	39 ($Z = +4.7$)	38.9 mm ($Z = +3.5$)
EF (BP) (%)	18	–	27	40	49	48
2-D LVGLS (%)	−7.5	–	–	−17	−20	−20.4
MR	Moderate	Moderate	Moderate	Moderate	Mild	Mild
RVD2 [mm]	6.8 ($Z = −4.9$)	15	13.3 ($Z = −0.2$)	15 ($Z = +0.5$)	22.5 ($Z = +2.9$)	19 ($Z = +1.4$)
TAPSE [mm]	12.5 ($Z = 0$)	10.8 ($Z = −2.3$)	11 ($Z = −2$)	14 ($Z = −1$)	12 ($Z = −2.2$)	16 ($Z = 0$)
FAC (%)	54	–	45	35	39	42
Δ p rPAB [mm Hg]		33	44	73	47	51

Δ p rPAB – pressure gradient across reversible pulmonary artery banding, FAC – fractional area change, EF (BP) – ejection fraction (biplane), LVDD – left ventricle diastole diameter, MR – mitral regurgitation, rPAB – reversible pulmonary artery banding, RVD2 – right ventricle mid cavity diameter, TAPSE – tricuspid annular plane systolic excursion, TEE – transoesophageal echocardiography, TTE – transthoracic echocardiography, 2-D LVGLS – 2-dimensional left ventricle global longitudinal strain

TABLE 2. Echocardiographic measurements in case 2 (M.A.)

TTE	Before rPAB	During procedure of rPAB (TEE)	At discharge	After rPAB 5 mo	After rPAB 11 mo	After rPAB 15 mo
LVDD [mm]	39 ($Z = +8.5$)	–	39 ($Z = +5.2$)	36 ($Z = +6.8$)	32 ($Z = +1.9$)	33 ($Z = +2.3$)
EF (BP) (%)	17	–	21	34	51	52
2-D LVGLS (%)	−8.6	–	–	−17	−25	−25
MR	Moderate	Moderate	Moderate	Moderate	Mild	Absent
RVD2 [mm]	8.3 ($Z = −3.5$)	14 ($Z = 0$)	14 ($Z = 0$)	12 ($Z = −1$)	15.4 ($Z = +0.9$)	16.6 ($Z = +1.2$)
TAPSE [mm]	13 ($Z = −1$)	9.1 ($Z = −3.3$)	11.8 ($Z = −2.3$)	13.6 ($Z = −1$)	13.4 ($Z = −1$)	15.4 ($Z = −1$)
FAC (%)	40	–	48	44	56	62
Δ p rPAB [mm Hg]		20	20	33	35	29

Δ p rPAB – pressure gradient across reversible pulmonary artery banding, FAC – fractional area change, EF (BP) – ejection fraction (biplane), LVDD – left ventricle diastole diameter, MR – mitral regurgitation, rPAB – reversible pulmonary artery banding, RVD2 – right ventricle mid cavity diameter, TAPSE – tricuspid annular plane systolic excursion, TEE – transoesophageal echocardiography, TTE – transthoracic echocardiography, 2-D LVGLS – 2-dimensional left ventricle global longitudinal strain
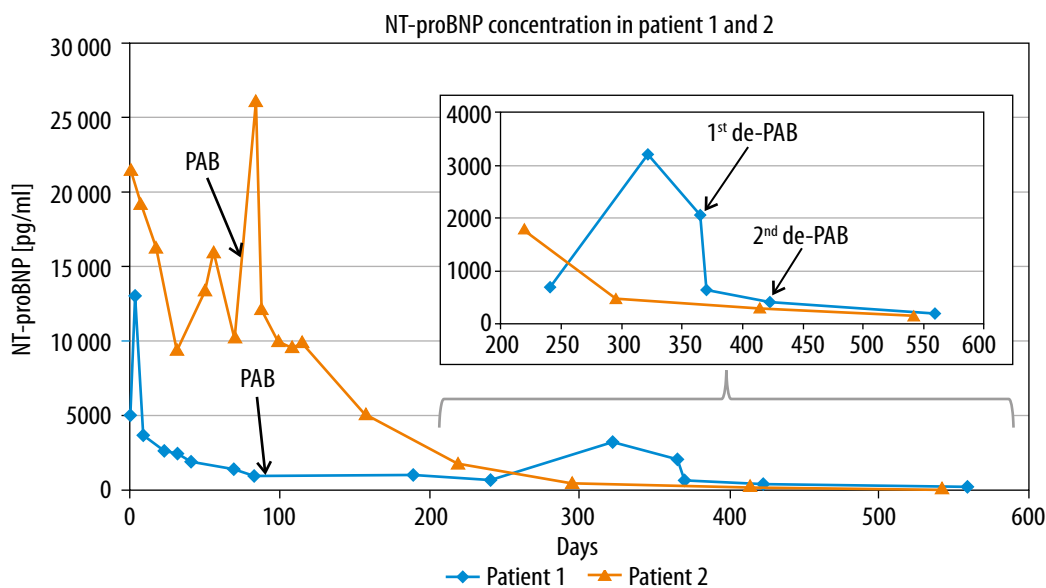
FIGURE 1. The value of NT-proBNP in study patients before and after reversible pulmonary artery banding

PAB – pulmonary artery banding placement, de-PAB – partial pulmonary artery debanding

by eye-ball assessment and measuring of right ventricle mid cavity diameter [RVD2]). Detailed echocardiographic data on hospital admission and during follow-up are presented in Tables 1 and 2.

CASES REPORTS

CASE 1

A 6-month-old male infant (M.B.) was transferred from regional hospital to our paediatric cardiology department with progressive symptoms of HF (Ross class IV). The boy was treated with oral HF medications (lisinopril, carvedilol, spironolactone, furosemide). From the age of 5 months his parents observed progressive lethargy and increased work of breathing. There was no recent history of respiratory infections. Family history of metabolic disorders and cardiomyopathies was negative. Initial TTE showed markedly enlarged LV with reduced EF and 2-D LVGLS and moderate mitral regurgitation (MR). The right ventricle was compressed by an enlarged LV, but RV systolic function was preserved. The value of NT-proBNP was highly increased. Viral polymerase chain reaction testing for myocarditis and metabolic tests results were negative. Genetic testing revealed that the patient is a heterozygous carrier of a new pathogenic molecular variant in the actin α cardiac muscle 1 (*ACTC1)* gene associated with the DCM phenotype. The patient received inotropic support in standard doses (dopamine, milrinone, one cycle of levosimendan infusion). The transcatheter atrial septostomy was performed to decrease left atrial pressure and pulmonary congestion. Because there was no improvement in the patient's clinical condition, he was qualified for rPAB. Shortly after the surgery it was possible to stop inotropic support and continue oral HF therapy. During first 5 months of fol-

low-up there were no considerable changes in LV and RV echocardiographic parameters, but there was significant clinical improvement (Ross class from IV to class II). During a routine follow-up visit, in TTE, an increase of pressure gradient across the PAB (60% above systemic arterial pressure) with deterioration of RV function was found. The partial PA debanding by the percutaneous balloon angioplasty was performed twice (on the 5th and 7th month) resulting in the establishment of optimal pressure gradient across the rPAB. After the procedure, improvement of RV function and normalization of NT-proBNP were observed (Figure 1).

In the further follow-up period, improvement in the clinical condition (Ross class I), LV systolic function (EF and 2-D LVGLS), and an increase of right ventricle mid-cavity diameter (RVD2) were noticed (Figure 2).

Weight changes of patient 1 treated with rPAB are presented in Figure 3.

CASE 2

A 8-month-old female infant (M.A.) was admitted to our paediatric cardiology department from a regional hospital with symptoms of end-stage HF (Ross class IV). She received inotropic support (milrinone, dopamine). In the previous 2 weeks she was hospitalized because of mild upper respiratory infection and diarrhoea of adenovirus aetiology. There was no family history of cardiomyopathy or metabolic diseases. Genetic testing revealed that the patient was a heterozygous carrier of a new pathogenic molecular variant in the myosin-binding protein C (MYBPC3) gene correlating with DCM. Metabolic tests results were negative. Initial TTE demonstrated LV dilatation, and reduced EF and 2-D LVGLS with moderate MR. The right ventricle was compressed by an enlarged left ventricle, but its systolic function was preserved. After
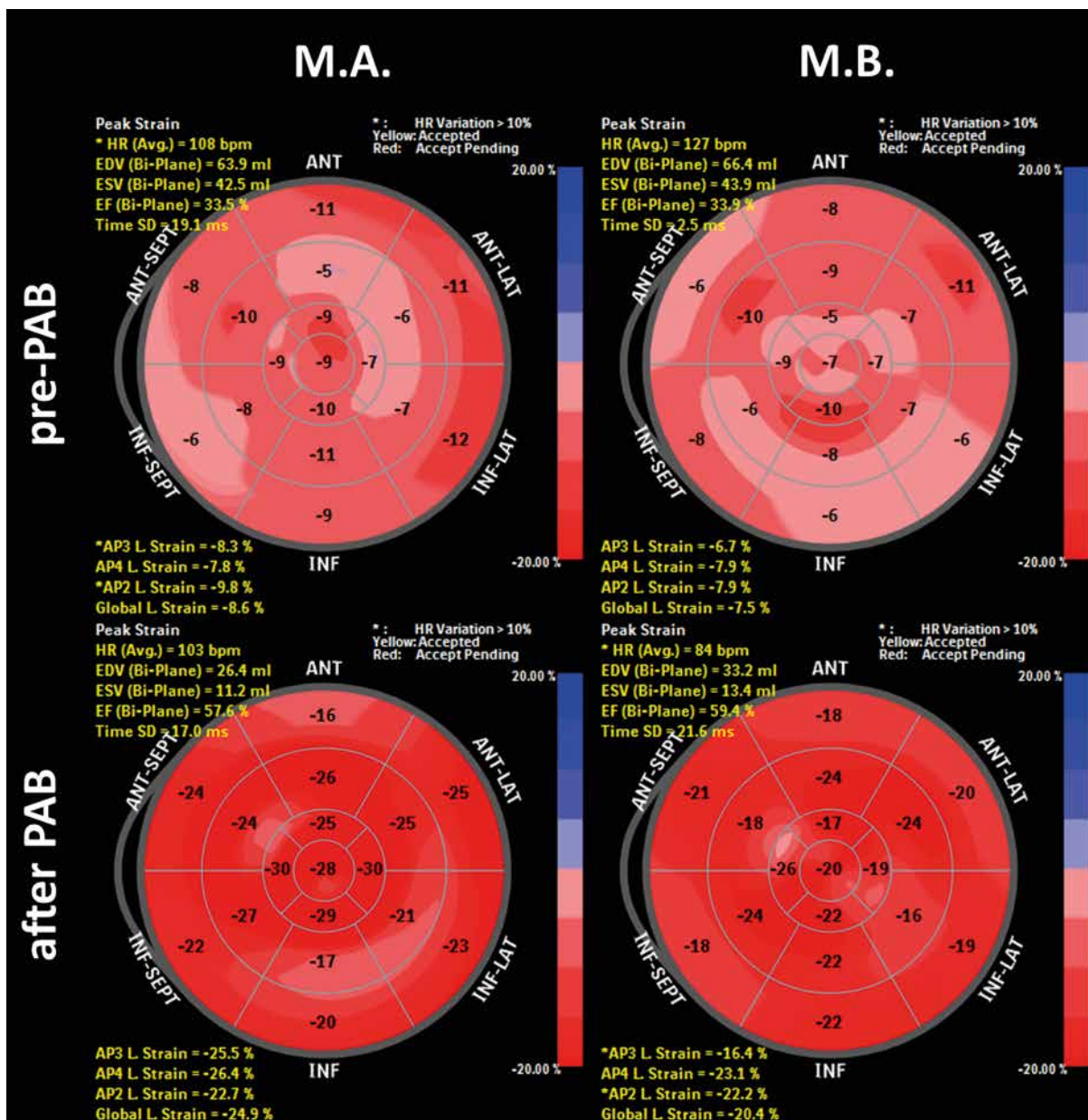
FIGURE 2. Assessment of left ventricular global longitudinal strain (bull's eye plot) before and after reversible pulmonary artery banding in a patient 1 (M.B.) – right panel [pre-rPAB (−7.5%), after rPAB (−20.4%)] and patient 2 (M.A.) – left panel [pre-rPAB (−8.6%), after rPAB (−25%)]

2 cycles of levosimendan infusion and continuous treatment with intravenous inotropic drugs, no significant clinical or echocardiographic improvement was observed. A rapid increase of NT-proBNP value was found. Patient was qualified for rPAB. During follow-up, a gradual improvement of LVEF and 2-D LVGLS was noted (Figure 2). The RV was less compressed by the LV and the RVD2 diameter increased. The significant decrease of NT-proBNP values and improvement of the patient's clinical status (Ross class I) were observed (Figure 1). Weight changes of patient 2 treated with rPAB are presented in Figure 3.

DISCUSSION

Dilated cardiomyopathy is the most frequent form of cardiomyopathy and a common cause of cardiac trans-plantation in the paediatric population. Literature reports indicate that 1- and 5-year rates of death or HTx were 31% and 46%, respectively [1]. The aetiology of child-hood DCM is highly heterogeneous, but the most common causes are myocarditis, and metabolic (including mitochondrial) and idiopathic cases. Genetic tests and application of a panel consisting of genes associated with DCM enables the identification of pathogenic variants in about 30–50% of patients [2].It should be emphasized that in both of our patients genetic tests showed the presence of pathogenic molecular variants correlating with DCM. Literature reports showed that risk factors for death or HTx in childhood DCM include age at diagnosis (< 4 weeks and > 5 years), the presence of familial DCM, and severity of LV systolic dysfunction at baseline [5]. Our patients, like the majority

of children with DCM, presented with severe congestive HF and high NT-proBNP values and were treated with ACE inhibitors, ß-blockers, mineralocorticoids, and less often diuretics, as recommended in the literature [6]. The ineffectiveness of pharmacological treatment prompted us to make further therapeutic decisions. In one child percutaneous transcatheter atrial septostomy and left atrial decompression were performed as a bridge to HTx or recovery, as described in the literature [7]. The concept of rPAB in end-stage DCM in children < 3 years of age was introduced by the Paediatric Heart Centre in Giessen [4]. The main aim of this treatment strategy is to support functional recovery of LV in DCM patients. Placement of PAB increases RV pressure, which gradually induces RV hypertrophy, and consequently, by shifting the interventricular septum towards the LV, it changes its morphology (from round to ellipsoidal) and improves LV systolic function. This surgical procedure was performed on both of our infants. It should be stressed that in echocardiography we observed a septal shift in both patients. Post-operatively, our patients underwent echocardiographic follow-up to assess myocardial recovery. It is particularly important to look for signs of RV pressure overload such as RV dilation or onset or worsening of tricuspid valve regurgitation. In such cases the PAB may be loosened in stages during a balloon catheter-based procedure to accomplish the optimal mild residual RV-PA pressure gradient of 15–30 mm Hg. In case 1, percutaneous loosening of the rPAB was performed twice. Based on our experience, we concluded that RVD2 will be the best parameter for assessment of the ventriculoventricular interaction. In both our cases the RVD2 diameter increased gradually during follow-up. Den Boer *et al.* [3] reported that, in paediatric DCM, 2-D LVGLS was a useful additional parameter and predictive of death and HTx. To our knowledge, this clinical report is the first in the literature which describes changes and improvement of 2-D LVGLS after rPAB. It should be noted that during 15 months of follow-up, clinical improvement, and a tendency for decreased NT-proBNP values and echocardiographic parameters were markedly improved (reduction of LVEDD, increasing of EF, 2-D LVGLS, and RVD2) in our patients.

CONCLUSIONS

Our early experience with rPAB in young children with end-stage DCM, like the results of other authors [4, 8, 9], indicates that this palliative therapeutic strategy is an effective alternative to mechanical support, HTx, and improves their clinical and haemodynamic status.

DISCLOSURE
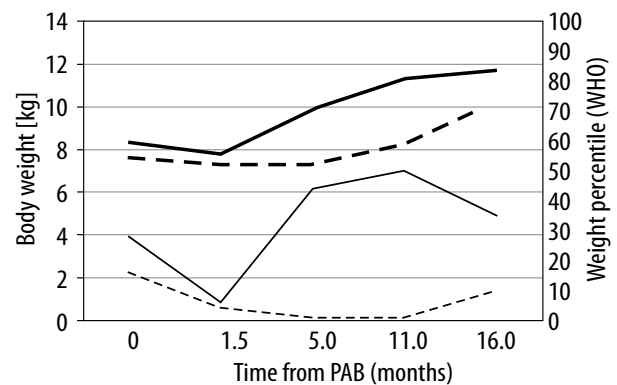
The authors declare no conflict of interest.

FIGURE 3. Weight changes of patients treated with reversible pulmonary artery banding. Continuous line — patient 1 (M.B.), interrupted line — patient 2 (M.A.). Thick lines — absolute body weight (kg), thin lines — weight percentiles according to World Health Organization standards

PAB – pulmonary artery banding placement, WHO – World Health Organization

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