Cardiology in the Young

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Levosimendan as a bridge to heart transplant in a 16-year-old patient with univentricular heart

Magdalena Mazurak, Paweł Cześniewicz and Jacek Kusa

Department of Pediatric Cardiology, Regional Specialist Hospital, Research and Development Center, Wroclaw, Poland

Abstract

We report the successful use of levosimendan in the treatment of heart failure in a patient with the univentricular heart. The presented case was atypical because our patient had systemic right ventricle. To our knowledge, it is the first reported such case with intermittent levosimendan administration as an effective treatment and bridge to successful heart transplant in a patient with functionally univentricular heart.

Brief Report

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Author for correspondence:
Magdalena Mazurak, MD, PhD, Wojewódzki Szpital Specjalistyczny, ul. Kamieńskiego 73a, 51-124 Wroclaw, Poland. Tel: +48691509787; Fax: +48713254101.
E-mail: madzia-mazurak@wp.pl

We present a 16-year-old patient with the hypoplastic left heart syndrome after Norwood procedure, hemi-Fontan procedure, transcatheter coil closure of major aortopulmonary collateral arteries and the both internal mammary arteries providing additional supply to the lungs. The patient met the criteria for the Fontan procedure in the early childhood, but the caregivers declined the proposed treatment and did not come for check-up visits for the next 11 years.

When the patient re-presented at age 16, he was in NYHA class III/IV heart failure, with a 6-minute walk distance 180 metres, ejection fraction 25% (Fig 1a and b) and N-terminal Prohormone of Brain Natriuretic Peptide-level 5279 pg/mL. He was treated with carvedilol, digoxin, enalapril, eplerenone, Furosemide, and warfarin. Progressive deterioration with acute worsening was observed resulting in recurrent monthly hospitalisations in our department. The patient was on the urgent heart transplant waiting list. During cardiac decompensation (Fig 2), the patient received an infusion of milrinone 0.5 ug/kg/minute for a few days but due to the lack of improvement we decided to add levosimendan, a potent non-adrenergic inodilator agent, a calcium sensitiser and potassium channel opener. Levosimendan enhances myocardial contractility by sensitising troponin C to ionic calcium. It acts without significant increase in oxygen consumption. Levosimendan also reduces afterload by opening adenosine triphosphate-sensitive vascular potassium channels (vasodilatory effect in arteries and veins).

Levosimendan was administered in repetitive doses, intravenous infusions started from December 2018, and our patient received a total of 12.5 mg of the drug once a month. Blood tests were performed prior to commencement of the infusion. No undesirable side effects were observed. The patient's condition and the exercise tolerance have slightly improved (longer distances – 6-minute walk distance 350 metres), N-terminal Prohormone of Brain Natriuretic Peptide levels decreased to 1896 pg/mL, and NYHA class decreased from III/IV to III during the follow-up. Unfortunately, the improvement in physical activity was not followed by an improvement in liver and kidney function parameters. Patient was still on the urgent heart transplant waiting list. During this entire period, he was never hospitalised due to decompensation. After 8 months of levosimendan treatment, orthotropic heart transplant was performed. The post-transplant outcome was uncomplicated.

Children with functionally univentricular heart represent the most demanding group of patients in paediatric cardiology. One of the most serious problems is the chronic heart failure. Current treatment includes combination of β-blockers, angiotensin-converting enzyme inhibitors, aldosterone antagonists, diuretics, and digoxin. Levosimendan has found its place in the treatment of acute decompensation of the chronic heart failure. Several clinical randomised controlled trials have demonstrated that levosimendan can be effective in the treating of adult patients with left ventricle failure. Intermittent levosimendan infusions in the advanced heart failure improved left ventricular function and favourably modulated neurohormonal activation.[1–3] Moreover, randomised trials in adults have found that levosimendan improves survival in comparison with conventional inotropes.[4,5] However, this only applies to two-chamber physiology, that is, left ventricular failure. In 2019, Tavares et al reported the successful use of levosimendan for acute decompensated heart failure in a 44-year-old patient with single ventricle (pulmonary atresia, previously submitted to three modified Blalock–Taussig shunts).[6] In 2020, Iacobelli et al. have described small case series of patients with hypoplastic left heart syndrome-like anatomy, levosimendan administration have improved contractility and optimised ventriculo–arterial coupling, with a reduction of heart rate.[7] Recently more interest is focused on the use of levosimendan in the treatment of the right ventricular failure.[8,9]

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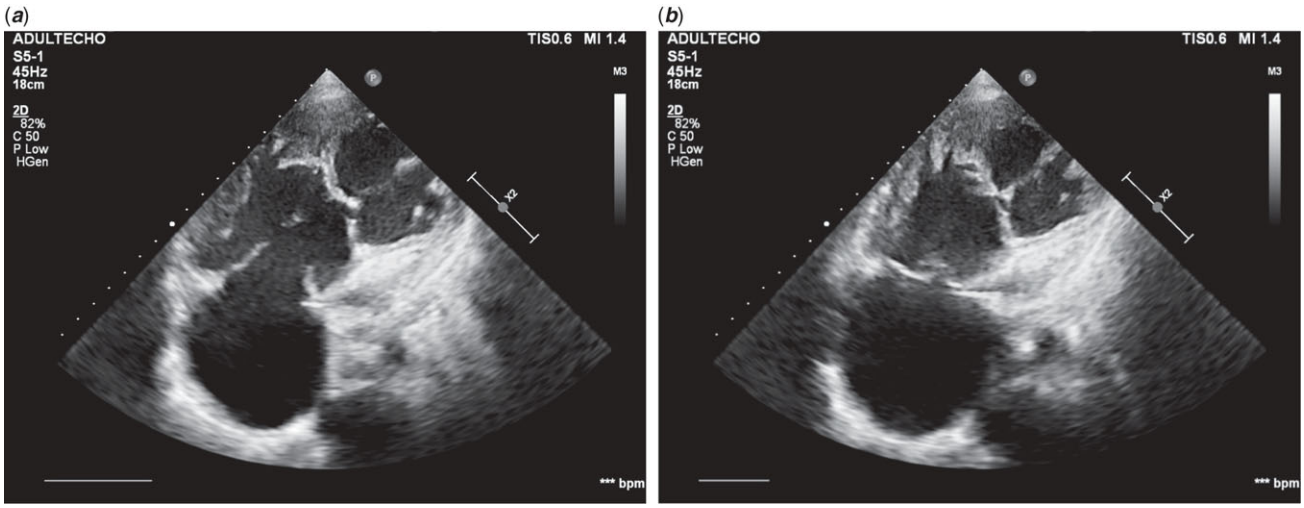

Figure 1. (***a*** and ***b***) Echocardiography, four-chamber view: diastole/systole (before levosimendan administration) shows significantly impaired single ventricle function.

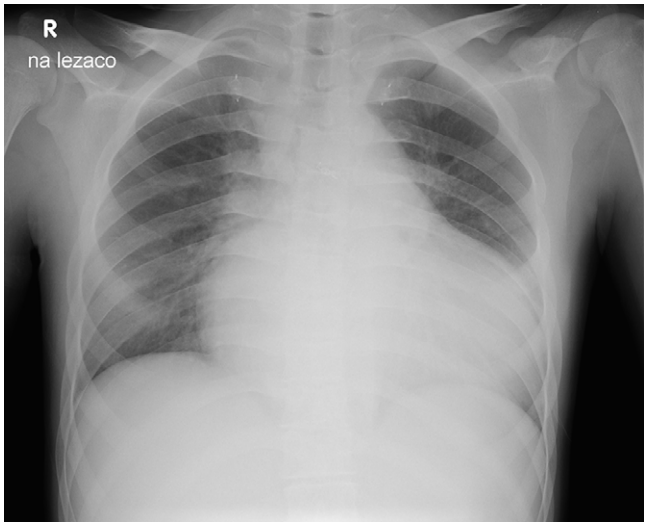

Figure 2. Chest X-ray exam (before levosimendan administration) shows significantly enlarged cardiac silhouette with pulmonary venous congestion.

Our patient had progressive heart failure, steadily increasing for several years. Echocardiographic parameters, assessing both systolic and diastolic functions, indicated critical myocardial damage and were steadily worsening with subsequent, more frequent hospitalisations caused by exacerbation of heart failure. During these hospitalisations, conventional adrenergic inotropes were often necessary. Any decompensation of chronic heart failure leads to permanent damage to part of the myocardium, which increases the risk of subsequent hospitalisation, as well as is a predictor of the risk of increased mortality. In addition, European Cardiac Society recommends the use of adrenergic inotropes in these patients only in a cardiogenic shock, since their excessive use can also have a negative impact on increased mortality (2016 The European Society of Cardiology Guidelines for the diagnosis and treatment of acute and chronic heart failure; despite the fact that these are guidelines developed for adult patients, due to the lack of such studies dedicated to children, they are also commonly used for the children's population).[10] In order to prevent these adverse effects, we decided to apply repeated "outpatient" doses of levosimendan. In this way, it was possible to stabilise the patient's condition, eliminate the need for hospitalisation due to exacerbation of heart failure, and reduce the risk of death due to heart transplantation.

We report the successful use of levosimendan in the treatment of heart failure in a child with the univentricular heart. The presented case was atypical because our patient had single ventricle physiology with a systemic right ventricle. Our case suggests that intermittent levosimendan administration can be effective treatment as a bridge to heart transplant in patients with functionally univentricular heart. To our knowledge, it is the first reported such a case. Levosimendan may prevent disease progression, reduce the need for repeated hospitalisation, and improve quality of life. Since this is the only one observed case, it cannot serve for any general conclusions. However, the use of levosimendan as a bridging therapy in patients with univentricular heart can be an attractive form of treatment for this group of the patients, regarding the high risk associated with the use of mechanical circulatory support and in the case of the lack of possibility of using a mechanical circulatory support.

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Conflicts of Interest. None.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Since this is a case report, no institutional review board approval was necessary.

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