Korean J Thorac Cardiovasc Surg 2017;50:378-381 □ CASE REPORT □
ISSN: 2233-601X (Print) ISSN: 2093-6516 (Online) https://doi.org/10.5090/kjtcs.2017.50.5.378

Large Atrial Septal Defect Closure in a Patient with Severe Pulmonary Arterial Hypertension

Supomo Supomo, M.D., Ph.D.[1], Anggoro Budi Hartopo, M.D., Ph.D.[2], Dyah Wulan Anggrahini, M.D., Ph.D.[2], Handy Darmawan, M.D.[1], Lucia Kris Dinarti, M.D., Ph.D.[2]

[1]Thoracic and Cardiovascular Surgery Division, Department of Surgery and [2]Department of Cardiology and Vascular Medicine, Dr. Sardjito General Hospital, Universitas Gadjah Mada

Patients with an atrial septal defect (ASD) and severe pulmonary arterial hypertension (PAH) are considered ineligible for defect closure surgery because of the risk of right ventricular decompensation and death after the operation. We report the case of a patient with large ASD and severe PAH who was able to undergo defect closure surgery successfully following long-term use of combined oral sildenafil and beraprost.

Key words: 1. Atrial heart septal defects
2. Beraprost
3. Congenital heart disease
4. Pulmonary hypertension
5. Sildenafil citrate

Case report

A 32-year-old female patient with a 5-year history of exertional dyspnea was referred to to Dr. Sardjito General Hospital. She presented with New York Heart Association (NYHA) class III exertional dyspnea without orthopnea or paroxysmal nocturnal dyspnea. Her vital signs were as follows: blood pressure, 100/60 mm Hg; heart rate, 90 beats per minute; and respiratory rate, 20 breaths per minute. Right ventricular heave and a wide, fixed, split S2 at the pulmonary valve area were found on a physical examination. Her walking distance was 357 m during a 6-minute walk test. A simple chest X-ray showed cardiomegaly and a dilated pulmonary trunk (Fig. 1). Electrocardiography revealed normal sinus rhythm with right axis deviation and right ventricular hypertrophy.

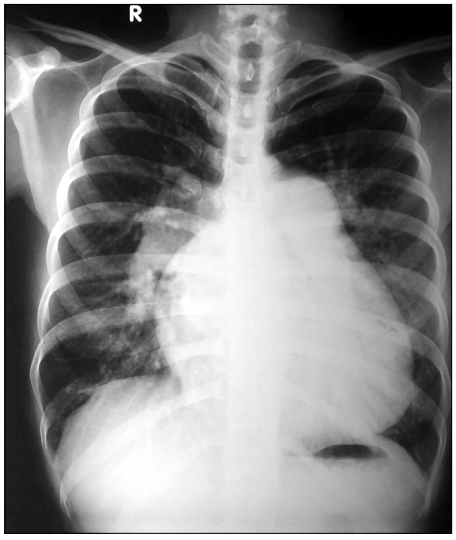

Fig. 1. Simple chest X-ray showing cardiomegaly and a dilated pulmonary trunk.

Received: April 12, 2017, Revised: June 5, 2017, Accepted: June 13, 2017, Published online: October 5, 2017

Corresponding author: Supomo Supomo, Department of Surgery, Faculty of Medicine, Dr. Sardjito General Hospital, Universitas Gadjah Mada, Sleman, Yogyakarta 55281, Indonesia
(Tel) 62-858-8072-8100 (Fax) 62-274-581333 (E-mail) supomo.tkv@mail.ugm.ac.id

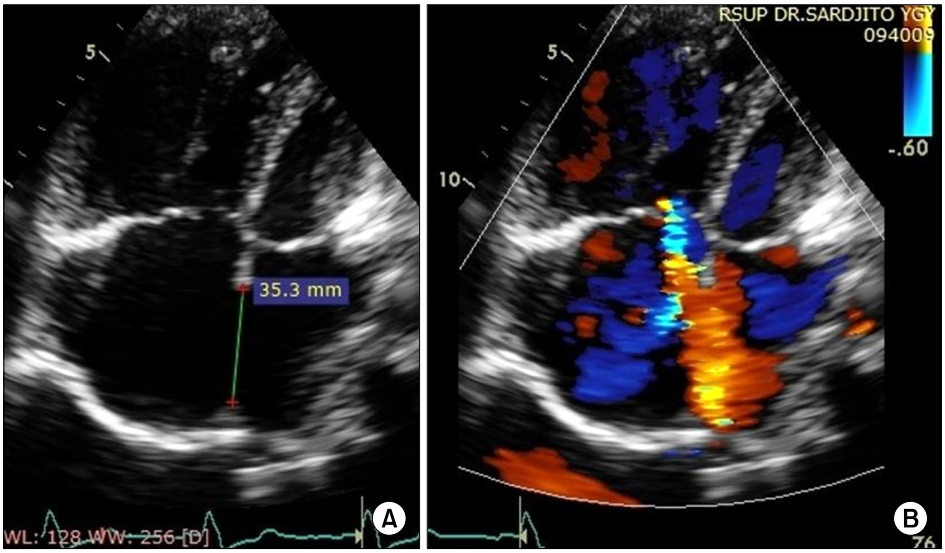

Fig. 2. (A, B) Transthoracic echocardiogram showing a large tissue defect of 35 mm, with a bidirectional shunt through the interatrial septum.

Transthoracic echocardiography (TTE) showed a large, 35-mm defect in the interatrial septum with a predominantly left-to-right bidirectional shunt (Fig. 2). The right ventricle and right atrium were markedly dilated, with a D-shaped left ventricle showing a normal ejection fraction and contractility. Cardiac catheterization indicated severe pulmonary arterial hypertension (PAH), with a mean pulmonary artery pressure (mPAP) of 77 mm Hg, baseline pulmonary vascular resistance (PVR) of 4 Wood units, and a systemic oxygen saturation level of 94%. Based on these findings, closure of the atrial septal defect (ASD) was not performed. Instead, medical treatment using oral sildenafil was started to reduce mPAP and PVR.

One year after starting the sildenafil therapy, the NYHA functional class of the patient improved from class III to II. The mPAP decreased from 77 to 50 mm Hg and was down to 44 mm Hg after a vasodilator test. In addition, PVR increased from 4 to 4.6 Wood units. We decided to add oral beraprost therapy to the patient's regimen. After 1 year of treatment using both oral sildenafil and beraprost, her symptoms and exercise tolerant were maintained at NYHA class II. She was able to walk 400 m during the 6-minute walk test and had a good oxygen saturation level of 97% at room air. The oxygen saturation level decreased slightly to 92% after the 6-minute walk test.

A follow-up TTE showed a reduction of mPAP from 50 to 38 mm Hg with a baseline PVR of 2.52 Wood units. Therefore, we decided to perform ASD closure surgery. After the surgery, the patient was given oral sildenafil; the dosage was 20 mg 3 times daily during the first month, and then reduced to 20 mg twice daily and once daily during the second and fourth month, respectively.

Four months after surgery, the patient's symptoms and exercise tolerance improved from NYHA class II to I. She was able to walk 439 m during the 6-minute walk test. No residual leakage was observed on the follow-up TTE. The diameters of the right atrium and right ventricle decreased from 55 to 19 mm and 53 to 24 mm, respectively, with normal contractility (Fig. 3). She was successfully weaned off sildenafil over a period of 6 months after surgery.

Discussion

Patients with ASD and an uncorrected left-to-right shunt are at risk for developing PAH. Persistent exposure to increased blood flow and pressure leads to vascular remodeling and dysfunction, resulting in a progressive rise of PVR and mPAP [1]. Patients with PAH have mPAP $\geq$25 mm Hg at rest or $\geq$30 mm Hg with exercise, pulmonary capillary wedge pressure $\leq$15 mm Hg, and PVR $>$3 Wood units. Mild, moderate, and severe PAH are defined by a mPAP between 25 and 45 mm Hg, between 46 and 65 mm Hg, and $>$65 mm Hg, respectively [2].

In patients with shunt-related PAH, the current practice is to perform a pulmonary vasodilator test to assess its reversibility. A decrease in mPAP or

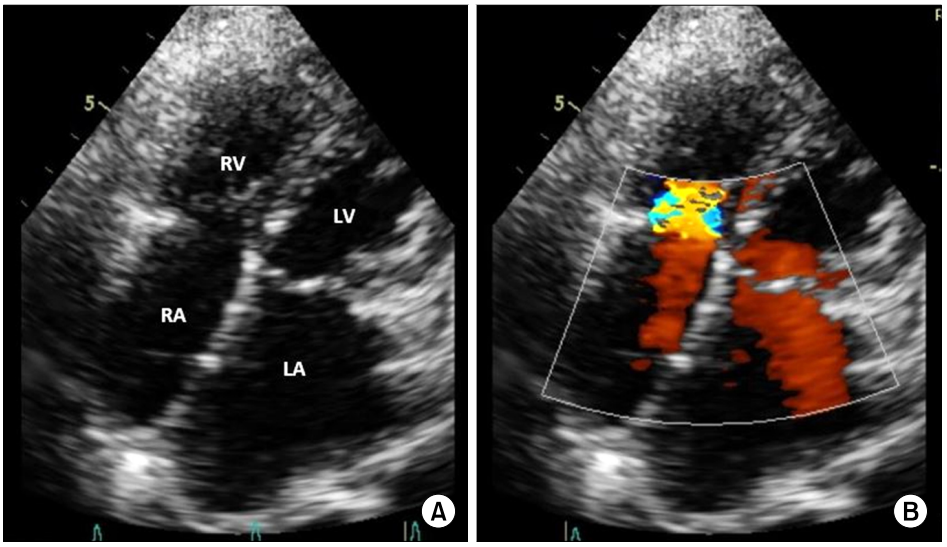

Fig. 3. (A, B) Transthoracic echocardiogram showing no residual leakage with normal RA, RV, LA, and LV diameters. RA, right atrium; RV, right ventricle; LA, left atrium; LV, left ventricle.

PVR that is less than 20% after a pulmonary vasodilator test indicates irreversible PAH [3]. Patients with severe or irreversible PAH are considered ineligible for defect closure, as the procedure is associated with a decrease in cardiac output, an increase in right-sided heart failure, and death in such patients [4,5].

The use of nonselective vasodilators that specifically target pulmonary vasodilation was reported to have a beneficial effect in patients with secondary PAH related to cardiac shunts [6,7]. Schwerzmann et al. [4] and Jung et al. [5] used 1-year intravenous prostacyclin and oral bosentan therapy, respectively, to treat ASD patients with less severe PAH. These patients showed clinical improvement after shunt closure following long-term vasodilator therapy. Our case illustrates that a similar result might be achieved in patients with more severe PAH if initially treated with sildenafil for 2 years and beraprost for an additional 1 year.

Sildenafil is a selective and potent inhibitor of phosphodiesterase type 5 that specifically degrades cyclic guanosine monophosphate in the pulmonary artery, which then acts to mediate smooth muscle relaxation of the vessel. Three randomized controlled trials demonstrated the safety and efficacy of sildenafil in improving mPAP, PVR, the cardiac index, and exercise tolerance in patients with PAH [7]. However, in our case, sildenafil alone was insufficient to reduce mPAP and to affect the reversibility of PAH. The mPAP remained moderately high and the PAH remained irreversible (<20% reduction of mPAP) after the vasodilator test and 1 year of therapy with oral sildenafil alone.

A systematic review demonstrated the effectiveness of a nonintravenous prostanoid (beraprost) in reducing the mortality of patients with severe PAH [6]. In our case, oral beraprost was combined with sildenafil, resulting in a marked reduction of mPAP and PVR. The value of PVR was within the normal range (<3 Wood units) and mPAP slightly increased [2]. The distance for the 6-minute walk test increased to the normal range of 380–782 m [8]. A follow-up 4 months after surgery showed a remarkable improvement of symptoms and exercise tolerance, from NYHA class II to I, with a walking distance of 439 m during the 6-minute walk test. No residual leakage was observed on the follow-up TTE. Furthermore, the function and diameter of the right atrium and right ventricle became normal (Fig. 3).

In conclusion, long-term combined sildenafil and beraprost therapy may offer the opportunity for ASD closure in situations where it was not previously considered feasible. This result also suggests that this therapy can be effective in the treatment of patients with shunt-related PAH.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Acknowledgments

We certify that this report is our own work and all source of information used in this report have been fully acknowledged.

References

1. D'Alto M, Mahadevan VS. *Pulmonary arterial hypertension associated with congenital heart disease*. Eur Respir Rev 2012;21:328-37.
2. Oliveira EC, Amaral CF, Moura MA, Campos FT, Pauperio HM. *Testing pulmonary vasoreactivity*. J Bras Pneumol 2008;34:838-44.
3. Tonelli AR, Alnuaimat H, Mubarak K. *Pulmonary vasodilator testing and use of calcium channel blockers in pulmonary arterial hypertension*. Respir Med 2010;104:481-96.
4. Schwerzmann M, Zafar M, McLaughlin PR, Chamberlain DW, Webb G, Granton J. *Atrial septal defect closure in a patient with "irreversible" pulmonary hypertensive arteriopathy*. Int J Cardiol 2006;110:104-7.
5. Jung IH, Lee SY, Lee SJ, et al. *Device closure of a large atrial septal defect in a patient with severe pulmonary arterial hypertension after 1 year use of an oral endothelin receptor antagonist*. J Cardiovasc Ultrasound 2013;21:140-4.
6. Ryerson CJ, Nayar S, Swiston JR, Sin DD. *Pharmacotherapy in pulmonary arterial hypertension: a systematic review and meta-analysis*. Respir Res 2010;11:12.
7. Barnett CF, Machado RF. *Sildenafil in the treatment of pulmonary hypertension*. Vasc Health Risk Manag 2006;2: 411-22.
8. Casanova C, Celli BR, Barria P, et al. *The 6-min walk distance in healthy subjects: reference standards from seven countries*. Eur Respir J 2011;37:150-6.