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Case Report

"Treat and Repair" Strategy for Atrial Septal Defect with Significant Pulmonary Arterial Hypertension in an Elderly Case

Oka S[1]*, Nakamura J[1], Tokumasu Y[1], Hoshino K[1], Watanabe K[1], Abe M[1], Akuzawa S[2], Suzuki K[2], Ishigami N[2], Sakai H[3] and Watanabe A[1]

[1]Department of Cardiology, Fujieda Municipal General Hospital, Japan

[2]Department of Cardiovascular Surgery, Fujieda Municipal General Hospital, Japan

[3]Department of Anesthesiology, Fujieda Municipal General Hospital, Japan

***Corresponding author:** Satoshi Oka, Department of Cardiology, Fujieda Municipal General Hospital, Surugadai 4-1-11 Fujieda, Shizuoka, Japan

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Abstract

Atrial Septal Defect (ASD) is relatively common in the population with adult congenital heart disease. It is sometimes complicated by Pulmonary Arterial Hypertension (PAH), and ASD closure in patients with significant PAH is controversial. However, recent advances in PAH-specific medications have improved PAH treatment and have led to a new treatment strategy that combines initial medical treatment of PAH with subsequent ASD closure (i.e., treat and repair strategy). The efficacy of this strategy has been reported and attracted attention. Transcatheter closure is preferred for repair rather than surgical closure because it is safer and less invasive. Thus, there are only a few reports of treat and surgical repair of large ASDs, especially in the elderly.

We present a case of an elderly patient with large ASD and significant PAH. Although he did not initially qualify for ASD closure, combination treatment with PAH-specific medications improved his hemodynamics, and surgical ASD closure was subsequently achieved. Finally, his World Health Organization functional class improved from class III to I.

Keywords: Atrial Septal Defect; Pulmonary Arterial Hypertension; Treat and Repair Strategy

Introduction

Atrial Septal Defect (ASD) is relatively common in patients with Adult Congenital Heart Disease (ACHD) [1]. Previous studies have shown the efficacy and safety of surgical or transcatheter closure of ASD in patients with mild Pulmonary Arterial Hypertension (PAH) [2-4]. However, ASD closure in patients with significant PAH remains controversial [5-6].

Recent advances in PAH-specific medications (Endothelin (ET)-receptor antagonists, Phosphodiesterase type 5 (PDE-5) inhibitors, and prostanoids) have been impressive [7]. These medications have improved the survival rate of patients with PAH associated with ACHD [8-11].

"Treat and repair" is a new therapeutic approach to ASD patients with PAH that combines PAH-specific medications with subsequent ASD closure [12]. Recent reports found that this strategy improved the World Health Organization Functional Class (WHO-FC), even in ASD patients with significant PAH [13].

We present the case of an ASD patient with significant PAH who was diagnosed at 66 years of age. Although PAH initially disqualified him for operative repair, combination therapy with PAH-specific medications made subsequent surgical ASD closure possible.

Case Presentation

A 66-year-old Japanese man had been diagnosed with chronic right Heart Failure (HF) with pulmonary hypertension 3 years prior to presentation. In his thirties, a heart murmur was discovered during a company health examination, but was not further investigated. He had been asymptomatic until he developed exertion dyspnea at 63 years of age. Despite starting diuretics, 60 μg/day of beraprost, and home oxygen therapy (3 L/min at rest), he developed lower extremity edema and dyspnea, and was referred to our hospital.

Upon admission to our hospital, physical examination revealed a blood pressure of 112/85 mmHg. A 12 lead electrocardiogram revealed atrial fibrillation with a rate of 140 bpm, right axis deviation, and right bundle branch block. Height was 159 cm and weight was 60 kg. On cardiac examination, a Levine III/VI systolic murmur was auscultated at the third left intercostal space close to the sternal border, and significant leg edema was observed. Blood examination showed polycythemia, decreased eGFR (46.1 ml/min/1.73m^2) and elevated brain natriuretic peptide (968 pg/ml). Serum levels of hepatobiliary enzymes were also elevated including total bilirubin (5.0 mg/dl), aspartate aminotransferase (41 IU/L), and γ-glutamyl transpeptidase (328 IU/L). A chest X-ray revealed cardiomegaly with pulmonary artery enlargement. Echocardiography revealed severe tricuspid regurgitation, with a pressure gradient of 42 mmHg. Left Ventricular (LV) wall motion was good, but the left ventricle showed a D-shape. LV diastolic dimension was 47 mm, and LV ejection fraction was 57%. ASD was suspected, but shunt flow was not clear (Figure 1A). ASD was diagnosed by transesophageal echocardiography (Figure 1B). The ASD was the secundum type, and its diameter was 40mm. Pulmonary embolism was not observed by computed tomography (Figure 1C) and lung ventilation-perfusion scintigraphy.

Systemic congestion was mildly reduced by administration

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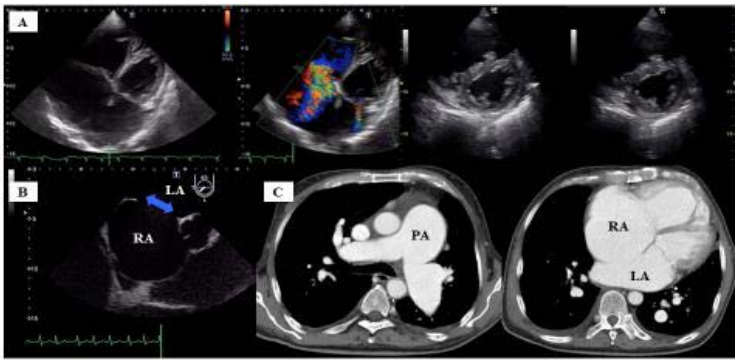

Figure 1: Cardiac examination at the first visit.
A: Echocardiography showed severe tricuspid regurgitation. Atrial septal defect was suspected, but the shunt flow was unclear. The left ventricle showed a D-shape.
B: Transesophageal echocardiography showed secundum atrial septal defect (blue arrow). (RA: right atrium, LA: left atrium)
C: Chest CT also showed secundum atrial septal defect and pulmonary artery dilatation. No pulmonary embolism was found. (PA: pulmonary artery, RA: right atrium, LA: left atrium).

Table 1: Clinical course of WHO-FC and cardiac examinations.

	At diagnosis	Time after institution of medication			After ASD closure		
		2 months	4 months		2 months	4 months	6 months
			Just before ASD closure	Just after ASD closure			
Systolic PAP [mmHg]	58	49	52	35	23	38	31
Mean PAP [mmHg]	50	37	29	25	18	26	18
PVR (mnHg/L/m)	9.4	3.9	3.1		1.8	3	1.7
PAWP [mmHg]	11	10	10		10	11	10
RAP [mmHg]	18	15	9		3	7	2
Systolic BP [mmHg]	87	94	104		100	93	106
Qp/Qs	1.6	2	1.6		1		1
WHO-FC	IV	III	III	III	II	II	II
BNP [pg/ml]	968	622	452		249	213	193
Body weight [kg]	60.6	55.1	51.7		50.3	53.2	53.5
6MWT [m]	100		290		310		410

PAP: Pulmonary Artery Pressure; PVR: Pulmonary Vascular Resistance; PAWP: Pulmonary Artery Wedge Pressure; RAP: Right Atrial Pressure; BP: Blood Pressure; WHO-FC: World Health Organization Functional Class; BNP: Brain Natriuretic Peptide; 6MWT: 6-Minute Walk Test.

of furosemide and tolvaptan. Heart rate was decreased to 90 bpm with diltiazem and low-dose digoxin. Cardiac catheterization was performed after the patient had stabilized. Coronary angiography showed no stenotic lesions. Swan-Ganz catheterization showed a mean Pulmonary Artery Pressure (mPAP) of 50mmHg, mean pulmonary artery wedge pressure of 11 mmHg, and Pulmonary Vascular Resistance (PVR) of 9.4 Wood units. Qp/Qs was 1.6. Based on this data, the diagnosis of ASD with PAH was confirmed. Although Eisenmenger Syndrome (ES) was ruled out, he was deemed inoperable due to significant PAH. However, after an oxygen load, mPAP and PVR decreased to 39 mmHg and 7.3 Wood units, respectively. Pulmonary vascular reactivity was observed, and we thus considered the possibility of "treat and repair".

PAH treatment was initiated with 40 mg/day of tadalafil. Subsequently, 5 mg/day of ambrisentan was prescribed. A month after discharge, he was readmitted for HF exacerbation. Beraprost was changed to 0.4 mg/day of selexipag and gradually increased to 1.2 mg/day. When the patient was stable 2 months after starting PAH treatment, cardiac Magnetic Resonance Imaging (MRI) was performed. Right Ventricular Ejection Fraction (RVEF) was 32.1%, and Qp/Qs was 2.0. Swan-Ganz catheterization was then performed, and Qp/Qs was also 2.0. PVR and mPAP had improved to 3.9 Wood units and 37 mmHg, respectively (Table 1). Based on these improvements, he was deemed a candidate for surgical ASD repair.

Surgical ASD closure was performed 4 months after the start of PAH-specific medications. A large (40 × 30 mm) ASD with lower perimeter edge defect was observed. It was closed with a 40-mm GORE TEX patch (W.L. Gore & Associates, Delaware, USA). Tricuspid annuloplasty (MC cube ring 32mm, Edwards Life Science, CA, USA) was also performed. Immediately after the operation, mPAP was 25 mmHg. We continued the PAH-specific medications.

The patient underwent Swan-Ganz catheterization at 2, 4, and 6 months after ASD closure, and his hemodynamic values were stable. At 6 months after ASD closure, mPAP was well controlled at 18mmHg (Table 1), and cardiac MRI showed significant reduction in RV end-diastolic volume (Figure 2). By that time, the patient's leg edema resolved and oxygen administration was no longer necessary. His 6-minute walk test improved from 100 meters to over 400 meters

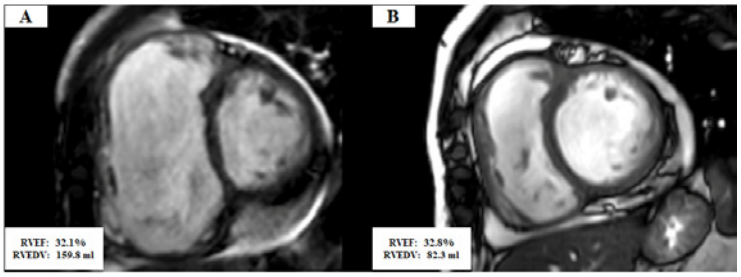

Figure 2: Cardiac MRI (end-diastole).
A: Two months after starting PAH treatment.
B: Six months after atrial septal defect closure, showing a significant reduction in Right Ventricular End-Diastolic Volume (RVEDV). There was no change in Right Ventricular Ejection Fraction (RVEF).

without shortness of breath. At 1 year after repair, his WHO-FC finally improved from class III to I. He continues to follow a good course.

Discussion

In ASD patients, Left-to-Right (L-R) shunt through the atrial septum increases pulmonary blood flow. In this case, there was slow progression of pulmonary artery endothelial dysfunction resulting in PAH. Thus, the patient was asymptomatic for over 60 years and was not diagnosed with ASD-PAH until the age of 66 years old. He did not qualify for ASD closure at the time of diagnosis. He was therefore started on combination therapy with PAH-specific medications. Medical treatment improved his hemodynamics, allowing for the possibility of ASD closure. In this elderly patient, the treat and repair strategy was successful, and both hemodynamic data and WHO-FC improved significantly.

Several points were considered regarding the selection of PAH-specific drugs. First, we prescribed ambrisentan, an ET-A selective antagonist, considering the patient's hepatopathy. Second, tadalafil, a PDE-5 inhibitor, was used because of his renal dysfunction and because of tadalafil's compatibility with ambrisentan [14]. It was previously reported that the combination of ET-A selective antagonists and PDE-5 inhibitors synergistically relaxed ET-1-induced pulmonary artery constriction, and this required functional ET-B receptors in the endothelium [15]. Third, we changed the prostanoid from beraprost to selexipag. Beraprost has beneficial effects in PAH progression, but its effects can decrease with long-term use [16]. Selexipag is an oral prostaglandin I2 receptor selective agonist. Its long-term effectiveness and safety have been demonstrated in patients with PAH [17]. Combination therapy with these drugs was effective in this case.

Hemodynamic data and RV function are key information before deciding to perform ASD closure. Yao recommended the following criteria for ASD closure: reduction of PVR to < 7.5 Wood units, reduction of mPAP to < 35 mmHg, preservation of RVEF (>40%), and predominant L-R shunt [18]. Our patient satisfied the criteria for PVR and mPAP, but had reduced RVEF even after treatment. Preserved RVEF is desirable, considering the possibility of a post-operative pulmonary hypertensive crisis. However, RVEF is not always improved by PAH-specific medications [19], and it has not been assessed in predicting operability in patients with PAH associated with ACHD. Thus, we performed surgical repair without waiting for improvement of RVEF. Although his systemic congestion temporarily worsened immediately after ASD closure, it was controlled with a continuation of PAH-specific medications and an increase in diuretics.

In ASD patients with significant PAH, transcatheter closure is preferred to surgery because it is less invasive. Takaya et al. reported that there was no difference in long-term outcome after transcatheter ASD closure in patients older than 75 years old and younger age groups [20]. Transcatheter closure is a valuable therapeutic option in elderly ASD patients. In this case, however, catheter closure was impossible due to a large ASD and its lower perimeter edge defect. Thus, surgical closure was performed.

In the REVEAL registry, the prognosis of PAH with congenital heart disease was still poor [21]. However, recently in Japan, initial upfront combination therapy with PAH-specific medications has become a standard strategy that has advanced the treatment of PAH [22]. Along with the trend, it is expected that more ASD patients with significant PAH will meet the criteria for ASD closure. In the era of combination therapy for PAH, the treat and repair strategy has the potential to improve the prognosis of unrepaired non-ES ASD patients with significant PAH.

Conclusion

Initial combination therapy with PAH-specific medications could allow for subsequent surgical closure of ASD, even in elderly patients with significant PAH.

References

1. Geva T, Martins JD, Wald RM. Atrial septal defects. Lancet. 2014; 383: 1921-1932.
2. Roos-Hesselink JW, Meijboom FJ, Spitaels SE, van Domburg R, van Rijen EH, Utens EM, et al. Excellent survival and low incidence of arrhythmias, stroke and heart failure long-term after surgical ASD closure at young age. A prospective follow-up study of 21-33 years. Eur Heart J. 2003; 24: 190-197.
3. Myers PO, Tissot C, Beghetti M. Assessment of operability of patients with pulmonary arterial hypertension associated with congenital heart disease. Circ J. 2014; 78: 4-11.
4. Yong G, Khairy P, De Guise P, Dore A, Marcotte F, Mercier LA, et al. Pulmonary arterial hypertension in patients with transcatheter closure of secundum atrial septal defects: a longitudinal study. Circ Cardiovasc Interv. 2009; 2: 455-462.
5. O'Donnell C, Ruygrok PN, Whyte K, Wilson NJ. Progressive pulmonary hypertension post atrial septal defect device closure-early symptomatic

improvement may not predict outcome. Heart Lung Circ. 2010; 19: 713-716.

6. D'Alto M, Romeo E, Argiento P, Correra A, Santoro G, Gaio G, et al. Hemodynamics of patients developing pulmonary arterial hypertension after shunt closure. Int J Cardiol. 2013; 168: 3797-3801.

7. Yao A. Recent advances and future perspectives in therapeutic strategies for pulmonary arterial hypertension. J Cardiol. 2012; 60: 344-349.

8. Berger RM, Beghetti M, Galie N, Gatzoulis MA, Granton J, Lauer A, et al. Atrial septal defects *versus* ventricular septal defects in BREATHE-5, a placebo-controlled study of pulmonary arterial hypertension related to Eisenmenger's syndrome: a subgroup analysis. Int J Cardiol. 2010; 144: 373-378.

9. Zhang ZN, Jiang X, Zhang R, Li XL, Wu BX, Zhao QH, et al. Oral sildenafil treatment for Eisenmenger syndrome: a prospective, open-label, multicentre study. Heart. 2011; 97: 1876-1881.

10. Mukhopadhyay S, Nathani S, Yusuf J, Shrimal D, Tyagi S. Clinical efficacy of phosphodiesterase-5 inhibitor tadalafil in Eisenmenger syndrome--a randomized, placebo-controlled, double-blind crossover study. Congenit Heart Dis. 2011; 6: 424-431.

11. Rosenkranz S, Ghofrani HA, Beghetti M, Ivy D, Frey R, Fritsch A, et al. Riociguat for pulmonary arterial hypertension associated with congenital heart disease. Heart. 2015; 101: 1792-1799.

12. Bradley EA, Chakinala M, Billadello JJ. Usefulness of medical therapy for pulmonary hypertension and delayed atrial septal defect closure. Am J Cardiol. 2013; 112: 1471-1476.

13. Kijima Y, Akagi T, Takaya Y, Akagi S, Nakagawa K, Kusano K, et al. Treat and Repair Strategy in Patients With Atrial Septal Defect and Significant Pulmonary Arterial Hypertension. Circ J. 2016; 80: 227-234.

14. Galie N, Barbera JA, Frost AE, Ghofrani HA, Hoeper MM, McLaughlin VV, et al. Initial Use of Ambrisentan plus Tadalafil in Pulmonary Arterial Hypertension. N Engl J Med. 2015; 373: 834-844.

15. Liang F, Yang S, Yao L, Belardinelli L, Shryock J. Ambrisentan and tadalafil synergistically relax endothelin-induced contraction of rat pulmonary arteries. Hypertension. 2012; 59: 705-711.

16. Barst RJ, McGoon M, McLaughlin V, Tapson V, Rich S, Rubin L, et al. Beraprost therapy for pulmonary arterial hypertension. J Am Coll Cardiol. 2003; 41: 2119-2125.

17. Sitbon O, Channick R, Chin KM, Frey A, Gaine S, Galie N, et al. Selexipag for the Treatment of Pulmonary Arterial Hypertension. N Engl J Med. 2015; 373: 2522-2533.

18. Yao A. "Treat-and-Repair" Strategy for Atrial Septal Defect and Associated Pulmonary Arterial Hypertension. Circ J. 2016; 80: 69-71.

19. Chin KM, Kingman M, de Lemos JA, Warner JJ, Reimold S, Peshock R, et al. Changes in right ventricular structure and function assessed using cardiac magnetic resonance imaging in bosentan-treated patients with pulmonary arterial hypertension. Am J Cardiol. 2008; 101: 1669-1672.

20. Takaya Y, Akagi T, Kijima Y, Nakagawa K, Sano S, Ito H. Long-term outcome after transcatheter closure of atrial septal defect in older patients: impact of age at procedure. JACC Cardiovasc Interv. 2015; 8: 600-606.

21. Barst RJ, Ivy DD, Foreman AJ, McGoon MD, Rosenzweig EB. Four- and seven-year outcomes of patients with congenital heart disease-associated pulmonary arterial hypertension (from the REVEAL Registry). Am J Cardiol. 2014; 113: 147-155.

22. Tamura Y, Kumamaru H, Satoh T, Miyata H, Ogawa A, Tanabe N, et al. Effectiveness and outcome of pulmonary arterial hypertension-specific therapy in Japanese patients with pulmonary arterial hypertension. Circ J. 2018; 82: 275-282.

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