Pulmonary arterial hypertension after atrial septal defect closure: a case report

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ABSTRACT

Most patients with congenital heart disease (CHD) who underwent successful shunts defect repair can be remained asymptomatic for years. It leads to a high number of losses to follow-up after patients discharge. After closure, pulmonary hypertension (PH) prevalence seems to be high and associated with increased morbidity and mortality. We reported a 55 y.o. female diagnosed with pulmonary arterial hypertension (PAH) and atrial fibrillation (AF) 31 years after atrial septal defect (ASD) closure by surgery, who never had routine follow-up evaluation because she remained asymptomatic for years. Physical examination revealed heart enlargement with irregular rhythm and pansystolic murmur in the fourth left sternal border. Electrocardiogram showed AF normal ventricular response, right axis deviation and suggestive for right ventricular hypertrophy. Laboratory testing found the NT pro-BNP level was 2,476 pg/mL. The chest X-ray showed enlargement of the heart and was representative of PH. From echocardiography study, transthoracic and transoesophageal echocardiography, we found no sign of residual shunt. There were right atrial and right ventricular dilatation, severe tricuspid regurgitation (TR) and a high probability of PH with TR velocity of 4.46 m/s. Right heart catheterization concluded mean pulmonary arterial pressure 46 mmHg, flow ratio 1.1, and pulmonary artery resistance index 15.5 Woods unit.m⁻². We highlight this case because of the high incidence of PH long after defect closure. The high number of lost to follow-up patients can lead to morbidity and mortality.

Keywords:
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INTRODUCTION

Congenital heart disease (CHD) with left-to-right shunt is one of the causes of pulmonary hypertension (PH) group 1 or pulmonary artery hypertension (PAH). The estimation of PH related to CHD in western countries is about 5-10%. In Indonesia, the prevalence data of CHD is still not available. Still, the data from the single centre show more than 1012 new CHD patients within five years of the registry, and most of them were atrial septal defect (ASD). For those with uncorrected left-to-right shunt CHD with PH have higher morbidity and mortality compared to others. If the shunt is left unrepaired, the risk of developing PH increased. However, the risk of PH after defect repair increased because of prior pressure and volume overload in the pulmonary vasculature.

The CHD associated with PAH (CHD-PAH) includes a condition after surgical or percutaneous shunt closure. The PAH can be developed immediately or recurred years after closure without signs of residual lesions after the procedure. Prognosis of patients who develop PAH after closure is worse than those with uncorrected CHD-PAH. This condition has caused concerns regarding repairing the defect in CHD patients with PAH. Here, we presented a case with PH, which developed several years after ASD closure by surgery.

CASE

A 55 y.o. female came to the PH clinic with shortness of breath with activity five years ago. The symptoms worsened in recent months and were followed by swollen legs. Because of her deteriorating condition, she consulted with a cardiologist and was referred to our hospital. She had been diagnosed with ASD and had performed defect closure by surgery when she was 24 y.o. Since there were no symptoms appeared after the surgery, she decided not to have regular follow-up evaluation.

The patient looked dyspneic during the current examination, with blood pressure 135/87 mmHg, heart rate 85 times/min, respiratory rate 20 times/min, and peripheral oxygen saturation 97%. Physical examination revealed an enlargement of the heart with irregular rhythm and pan systolic murmur best heard in the fourth left sternal border.

The electrocardiogram (FIGURE 1) showed atrial fibrillation with a normal ventricular response, right axis deviation, right ventricular hypertrophy and non-frequent ventricular extrasystole. The laboratory investigation demonstrated a haemoglobin level of 13.6 g/dL, and white blood cells count 11.48 × 10³/µL, platelet count of 237× 10³/µL, creatinine level 1.14 mg/dL, blood glucose 116 mg/dL and NT pro-BNP level of 2,476 pg/mL. The chest X-ray (FIGURE 2) showed enlargement of the heart with cardiothoracic ratio (CTR) > 0.65 and suggestive for PH.
FIGURE 1. Electrocardiography of patient

FIGURE 2. Chest X-ray of patient
The transthoracic echocardiography (FIGURE 3) showed right atrial and right ventricular dilatation, left ventricle D-shaped, left ventricular ejection fraction (LVEF) 70%, no residual ASD, severe tricuspid regurgitation (TR) and high probability of PH with TR velocity 4.46 m/s. The transoesophageal echocardiography revealed interatrial septum (IAS) and interventricular septum (IVS) were intact and no residual shunt with severe TR. In the 6-min walk test, she walked 160 m.

The patient proceeded to get right heart catheterization (RHC). The result of RHC indicated increased mean pulmonary artery pressure (mPAP) as high as 46 mmHg, flow ratio (FR) 1.1 and pulmonary artery resistance index (PARI) of 15.5 Woods unit.m⁻². The patient was diagnosed with PAH after ASD closure and currently atrial fibrillation normal ventricular response. She was treated with oral sildenafil 20 mg t.i.d, oral digoxin 0.25 mg q.i.d and warfarin 2 mg q.i.d at night. After treatment, she showed an improvement in functional class. She also demonstrated an increased distance in the 6-min walk test (435 m). The level of NT pro-BNP decreased to 1,070 pg/mL. There is also no sign of the adverse effect of sildenafil. The result from regular follow-up is shown in TABLE 1.

### DISCUSSION

Pulmonary hypertension is explained as an mPAP >20 mmHg. In comparison, PAH is a pulmonary vascular disease that is described by mPAP >20 mmHg, pulmonary capillary wedge pressure (PCWP) <15 mmHg and pulmonary vascular resistance (PVR) > 3 Woods unit as assessed by RHC.⁵,⁶ A PH related with congenital heart disease with a left to right shunt is admitted in group 1 of the classification of PH or PAH.⁷ A CHD-PAH on the patients with ASD with significant left to right shunt, with Qp/Qs >1.5, signs of right ventricular overload, PVR <5 Woods unit and PVR/SVR <0.3 should be closed regardless of the symptom.⁸ This
defect can be repaired either by surgery or device depend on the type of ASD and eligibility for closure.9

Our patient was diagnosed with ASD secundum and had closure by surgery when she was 24 y.o. Unfortunately, we do not have data before surgery from her earlier hospital. After surgery, she never had routine follow-up examinations. Since last year she became easily tired and had shortness of breath. The 2015 European Society of Cardiology Guidelines about Diagnosis and Management of PH recommend that the CHD-PAH be grouped into 4, namely Eisenmenger’s syndrome, PAH related with prevalent systemic-to-pulmonary shunts, and PAH with small/coincidental defects and PAH after defect correction.10

This patient could be classified in the last group, where the PAH persisted instantly after closure or developed months or years later. She had had ASD closure by surgery in adolescence and remained asymptomatic decades later. D’alto et al.4 stated PH might develop or become symptomatic years after shunt closure in people with PVR >5 Woods unit, PVRI >6 Woods unit.m², and PVR/SVR >0.33. Unfortunately, we did not have the patient’s data before operated because this patient was surgeried in another hospital 31 y.o.4

German National CHD Registry reported PH prevalence of 3.0% among 825 simple lesions such as ASD, VSD and PDA patients that have already been corrected. In that study, symptomatic PH developed after a median follows up of 15.9 years after shunt repair. The mean age at the time of closure was higher in the PH group compared to the no PH group. Patients with PH had a higher morbidity and mortality risk. In confirming the diagnosis of PH, it is recommended to life-long monitoring and low threshold for examination, which has a significant clinical and prognostic purpose. This study also showed that the prevalence of PH was increased mainly after 50 years of life. The highest PH risk was found in the group of PDA patients, followed by ASD and VSD.9

In a systematic review and meta-analysis evaluating PH prevalence after ASD closure percutaneously, they reported a decrease in the prevalence of PH from 44 to 18% after closure procedures at a mean follow-up of 15-60 months. They also reported a significant variation in the PH prevalence among the literatures reviewed, with the highest prevalence being found in studies with small samples. This systematic review involving 15 studies showed that there is still a decline in PH prevalence until 60 months of follow-up after ASD closure.11

Another systematic review and meta-analysis studying PAH prevalence in ASD before and after ASD closure (surgical or percutaneous) at adult age reported that prevalence of PAH before ASD closure ranged from 29-70% and 5-50% after closure within a mean follow-up range of 13-98 months. After closure, the PAH prevalence in ASD is considered highest in studies with older dates, small study cohorts with small sample sizes, and studies with high follow-up loss. A sensitivity analysis was conducted excluding all high numbers of a follow-up loss study, which resulted in the prevalence of PAH 42 and 16% in ASD before and closure, respectively. This study also mentioned a significant reduction of mean PAP, which is 34±10 before closure and 28±10 after closure.12

The follow-up of patients with post ASD closure should evaluate a residual shunt, right ventricle dimension and function, TR and estimated PAP by echocardiography. The diagnosis of arrhythmia by electrocardiography and Holter evaluation is essential. Those with residual shunt increased mPAP or arrhythmias. Those repaired at adults age should undergo routine follow up assessment for the first two years depending on the result; every 3-5 years is reasonable.9 Another
guideline stated that physiological and haemodynamically stable patients could be assessed for routine follow up every 2-5 years. But for moderate and severely ill patients should have more frequent follow-up evaluations (including history, electrocardiography, echocardiography, pulse oximetry and exercise test) about every 3-12 months depends on the result.\(^\text{13}\)

Until now, there are no specific guidelines that recommend how long the total duration of follow-up evaluation should be conducted in ASD patients after closure. Even so, there is a report from the Dutch Congenital Corvitia registry mentioned that from 1.103 patients with the shunt (474 of them are ASD), there is a total incidence of PH shortly after repair for 2.1\%(95\% CI:0.3-0.77) and >15\% (95\% CI:2.6-23.8) 50 years after repair. This report explains the progress of PH after shunt closure.\(^\text{14}\) The progression of PH is possible because of the excess volume and pressure resulting in damage to the pulmonary vessels, which in time lead to PH.\(^\text{15}\) There are some studies mentioning risk factors of PH development after ASD closure. Patients with ASD closure at older age (especially >40 y.o.) are more likely become PH. As well as those with residual shunt, elevated PAP or arrhythmias should be evaluated regularly.\(^\text{9}\)

**CONCLUSION**

We reported a 55 y.o. female diagnosed with PAH and atrial fibrillation 31 years after ASD closure by surgery. This condition is possible because PAH can be found and developed over time after closure. PAH can occur immediately or years after surgery. Therefore, routine and careful follow-up evaluation after defect closure is needed.

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**REFERENCES**

1. Diller GP, Gatzoulis MA. Pulmonary vascular disease in adults with congenital heart disease. Circulation 2007; 115(8):1039-50. [https://doi.org/10.1161/CIRCULATIONAHA.105.592386](https://doi.org/10.1161/CIRCULATIONAHA.105.592386)


6. Humbert M, Montani D, Evgenov...
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OV, Simonneau G. Definition and classification of pulmonary hypertension. Handb Exp Pharmacol 2013; 218:3-29. https://doi.org/10.1007/978-3-642-38664-0_1


