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**CASE REPORT**

# Management in Mitral Valve Replacement with Pulmonary Hypertension and Thyroid Storm: A Case Report

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## ABSTRACT

**Introduction:** We reported a case of patient after mitral valve replacement (MVR) with pulmonary hypertension (PH) and thyroid storm that is rare, but life-threatening condition.

**Case Illustration:** A 57-year-old-male with a subclinical hyperthyroidism underwent MVR due to severe mitral regurgitation (MR) and high possibility for PH. He showed atrial fibrillation with normal left ventricular ejection fraction (LVEF). In the intensive care unit (ICU), four hours postoperatively, he developed thyroid storm with heart rate of 226 times/min, temperature 39ºC, and thyroid function showed low TSH (<0.05 uIU/mL), high fT4 (25.4 pmol/L), and high T3 (3.3 nmol/L). He was administered with propranolol, propylthiouracil, hydrocortisone, and lugol.

**Discussion:** Trauma of cardiac surgery might trigger thyroid storm in this patient. The post-operative period represented a high-risk time for PH patients, moreover with thyroid storm. Therapy for thyroid storm was multimodal, including anti-thyroid, beta blockers, iodine, and glucocorticoid. Hemodynamic goals were avoidance of elevation in pulmonary vascular resistance (PVR), avoidance of myocardial depressants and maintenance of systemic vascular resistance (SVR), myocardial contractility and preload.

**Conclusion:** Thyroid storm and PH complicating MVR was rare, but life-threatening. Comprehensive management could decrease morbidity and mortality of thyroid storm.

**Keywords**: mitral valve replacement surgery; pulmonary hypertension; thyroid storm

## INTRODUCTION

The Global, Regional, and National burden of rheumatic heart disease (RHD) in 1990–2015 showed that Indonesia was estimated as the fourth ranked countries with the largest estimated numbers of RHD cases (1.18 million cases) in 2015, following after India (13.17 million cases), China (7.07 million cases), and Pakistan (2.25 million cases).[1] Most patients with RHD was preferred to undergo mitral valve surgery, particularly mitral valve replacement (MVR), with thirty-day mortality 0.7% for MVR with aortic valve replacement (AVR).[2]

Pulmonary hypertension (PH) is an increased mean pulmonary arterial pressure (PAPm) ≥25 mmHg at rest as assessed by right heart catheterization (RHC) due to multiple aetiologies.[3, 4] PH after MVR leads to an increased risk of mortality and morbidity. The cardiovascular and disease complexity makes difficulties to find a specific reason for the high operative mortality. The mortality of a MVR surgery in patients with RHD with a concurrent pulmonary arterial hypertension (PAH) accounts for 15 to 31%. Persistent PH was present in 42.3% of patients after 12.6 months of mean follow-up.[5] PH after MVR was more frequently observed in elderly and female patients, in those with severe degrees of PH before surgery, significant degrees of tricuspid regurgitation (TR), and smaller prosthetic size.[5]

European Society of Cardiology (ESC) and European Respiratory Society (ERS) Guidelines 2015 classified the second group of PH class as the PH due to left heart disease, such as valvular heart disease, and also classified the fifth group of PH class as the group of PH with unclear multifactorial mechanisms, includes patients with thyroid disorders.[4]

Thyroid disease in patients with cardiac disease, either valvular or coronary, is also a common finding. While hyperthyroidism itself affects an estimated 2.1% of the population.[6] Its prevalence depends on the nature of thyroid disease, patients' age, frequency of screening as well as concomitant cardiac medications that affect thyroid metabolism. Thyroid dysfunction affects cardiovascular physiology by different means, including myocardial inotropy, heart rate, cardiac output, and peripheral arteries reactivity. A mildly altered thyroid status is associated with an increased risk of mortality in patients with cardiac disease.[7] There were higher cardiac death and overall death in subclinical hyperthyroidism (8.2% and 9.2%) in comparison with euthyroidism (3.4% and 7.3%) after mean follow-up of 32 months.[7] Survival rates for cardiac death were lower in subclinical hyperthyroidism than in euthyroidism.[7]

Thyroid storm (TS) is a rare, severe, life-threatening endocrine condition characterized by severe clinical manifestations of decompensated thyrotoxicosis. It represents an extremely elevated circulating thyroid hormone concentrations. It is one of thyroid emergencies and associated with increased mortality and poor prognosis.[8, 9] TS often develops out of a long-standing undiagnosed or untreated hyperthyroidism, precipitated by an acute stress-associated event, such as infection, trauma, thyroid or non-thyroid surgery, diabetic

ketoacidosis, radioiodine therapy, severe emotional stress, and pregnancy or delivery.[9, 10]

Although the exact incidence of TS in Indonesia is unknown, a national survey from Japan estimated an incidence of TS in hospitalized patients to be 0.20 per 100,000 patients, per year.[9] In Japan, TS carries a mortality rate of 10%, while thyrotoxicosis without TS carries a mortality rate of 0%.[9] Multiple organ failure (MOF) was the most common cause of death in TS, followed by congestive heart failure (CHF), respiratory failure, cardiac arrhythmia, disseminated intravascular coagulation (DIC), gastrointestinal perforation, hypoxic brain syndrome, and sepsis.[9]

The diagnosis of TS is mostly made based on clinical symptoms criteria, as thyroid hormone measurements do not differentiate between TS and uncomplicated hyperthyroidism. In order to make a prompt diagnosis of TS, several cardinal criteria were used including hyperthermia, cardiovascular symptoms or heart rate, in particular tachycardia or atrial fibrillation, central nervous system dysfunction symptoms, signs of CHF, gastrointestinal symptoms, myasthenia, and any precipitating events.[9, 11]

TS must be immediately identified and managed in order to prevent major complications. Management of TS requires both medical and supportive therapies and requires an intensive care unit setting.[8] Medical treatment is intended to inhibit the thyroid hormone synthesis and secretion (antithyroid drugs such as propylthiouracil (PTU) or methimazole, perchlorate, lugol's solution, cholestyramine, or thyroidectomy) and inhibit the thyroid hormone effects in the periphery (beta -blockers, glucocorticoids).[10, 12]

Since open-heart surgery such MVR may cause a thyrotoxicosis crisis during the perioperative period in patients with hyperthyroidism, close monitoring and control are needed. Here we reported a case of management of patient after MVR surgery with PH and TS, in which to our knowledge, this was the first case report of a patient with TS after MVR surgery.

## CASE ILLUSTRATION

A 57-year-old male came to cardiology out-patient clinic with chief complaint of worsening shortness of breath for seven years with typical symptoms and signs of heart failure due to RHD. In addition to uncontrolled hypertension, he also has a history of subclinical hyperthyroidism and received thyroid treatment since April 2018. Routine treatments were furosemide 10 mg/24 hours, ramipril 5 mg/24 hours, bisoprolol 5 mg/24 hours, spironolactone 12.5 mg/24 hours, and propylthiouracil 100 mg/24 hours.

In the out-patient clinic, his cardiac examination showed that the cardiac apex shifted to caudolateral. His cardiac auscultation showed loud pansystolic murmur at the apex and increased jugular vein.

In admission, he was noted to be afebrile, irregularly irregular heart rate of 84 beats/min and normal blood pressure of 130/80 mmHg. No goiter was detected at that time. There were no specific clinical manifestations of Graves' disease such as thyroid eye disease (ie, exophthalmos, lid lag), a diffuse goiter with a bruit, dermopathy, or thyroid acropachy (ie, digital clubbing and swelling). The results of other physical examination were non-specific for hyperthyroidism. The signs and symptoms of thyrotoxicosis such as heat intolerance, diaphoresis, tremors, anxiety, fatigue, severe weight loss, hyper-reflexia, and warm and moist skin were not specifically appeared. There was no coexistence of other autoimmune diseases in the patient or the patient's family.

Laboratory studies revealed a subclinical hyperthyroidism phase: serum triiodothyronine (T3) 3.3 nmol/L, serum free thyroxine (fT4) 25.4 pmol/L, and thyroid-stimulating hormone (TSH) levels <0.05 mIU/L. His electrocardiogram (ECG) showed atrial fibrillation with normal ventricular response and his thorax x-ray showed cardiomegaly with left atrium and left ventricle enlargement. Transthoracic echocardiogram (TTE) demonstrated left atrial dilatation, eccentric hyperthrophy of left ventricle, left ventricle systolic function of LVEF 68%, severe mitral regurgitation (MR), mild tricuspid regurgiation (TR) and intermediate probability for PH. From all examination results, the patient was sent for MVR surgery.

During the induction of anesthesia, 5 mg of midazolam, a high dose of fentanyl was administered to prevent thyrotoxicosis and cardiac depression. Venous access points were peripheral intravenous (IV), subclavian central venous catheterization (CVC) and side ports via the internal jugular vein. Intraoperative monitorings were using automated non-invasive blood pressure (NIBP), arterial blood pressure (ABP), pulse oxymetry, electrocardiography (ECG), End Tidal CO2, core temperature, central venous pressure (CVP) and transesophageal echocardiography (TEE).

Cardiac surgery through a median sternotomy was performed. The patient underwent MVR with cardiopulmonary bypass (CPB). The patient was not febrile intraoperatively. The maximal patient temperature during surgery was 36$^{o}$C. The surgery was completed with a surgery duration of 120 minutes, an aortic cross clamp duration of 55 minutes, and CPB duration of 65 minutes. All intraoperative hemodynamic data were recorded as in Table 1.

Patient was transferred to the ICU and supported by mechanical ventilation with SIMV mode, tidal volume 450 ml, PEEP 5, FiO2 50%, and rate of 14. The drugs delivered through syringe pump were dobutamine, milrinone, nitroglycerin, midazolam, and morphine. The dosage of the drug depend on the patient's hemodynamics. Patient was given maintenance crystalloid as much as 50% of the total fluid needs per day. Some of these treatments were intended for the PH management that aimed to avoid elevations in pulmonary vascular resistance (PVR), to maintain systemic vascular resistance (SVR), to avoid myocardial depressants and to maintain myocardial contractility, preloads and normal sinus rhythms if possible. Other injection drugs were meropenem, omeprazole, ondansetron, calcium gluconate, and paracetamol. Complete laboratory tests, chest x-ray, and echocardiography have been requested.

After 4 hours postoperatively, the patient experienced a TS with clinical symptoms of altered mental status (delerium), tachycardia (atrial fibrillation with rapid ventricular response), and hyperthermia with hemodynamic

data as in Table 2. After diagnosis, early multimodal treatments, including treatments for the precipitating event, supportive treatments and close monitoring were initiated. During TS, 80 mg/8 hour propanolol, propylthiouracil 200 mg/4 hours, hydrocortisone 100 mg/8 hours and lugol 8 drops/6 hours were administered. Patient was still supported by mechanical ventilation until 24 hours recovery from TS.

The perioperative and postoperative serum levels of thyroid hormone and thyroid-stimulating hormone are shown in Table 3. The most normal levels of thyroid hormone was found after postoperative day 3. Patient was extubated in the ICU in postoperative day-3. He was transferred to the ward after postoperative day-5 and discharged without symptoms on postoperative day-7. He was discharged on oral methimazole and tapering dose of steroids. The patient continues to remain euthyroid and asymptomatic in the most recent cardiovascular clinic follow up.

Table 1. Intraoperative Hemodynamic Data

| Minute to | MAP | HR | T | RR | SpO2 | $ETCO_2$ | CVP |
|---|---|---|---|---|---|---|---|
| 15" | 78 | 80 | 36.2 | 14 | 100 | 36 | 16 |
| 30" | 72 | 64 | 35.8 | 12 | 100 | 32 | 14 |
| 45" | 74 | 60 | 35.2 | 12 | 100 | 28 | 11 |
| 60" | 68 | 62 | 35.4 | 12 | 100 | 25 | 11 |
| 75" | 70 | 53 | 35 | 12 | 100 | 26 | 8 |
| 90" | 69 | - | 32.2 | - | - | - | - |
| 105" | 64 | - | 30.1 | - | - | - | - |
| 120" | 75 | - | 31.2 | - | - | - | - |
| 135" | 72 | - | 30.4 | - | - | - | - |
| 150" | 65 | 112 | 34.6 | 12 | 100 | 30 | 8 |
| 165" | 74 | 96 | 35.6 | 12 | 100 | 34 | 9 |
| 180" | 71 | 98 | 35.8 | 12 | 100 | 28 | 12 |

Abbreviation: MAP (mean arterial pressure), HR (heart rate), T (temperature), RR (respiration rate), SpO2 (peripheral oxygen saturation), ETCO2 (End Tidal CO2), CVP (Central Venous Pressure), - (on Cardiopulmonary Bypass)

Table 2. Postoperative Hemodynamic Data in the ICU

| Time | MAP | HR | T | RR | $SpO_2$ |
|---|---|---|---|---|---|
| 17.00 | 100 | 112 | 37.3 | 12 | 100 |
| 17.30 | 101 | 121 | 37.9 | 12 | 100 |
| 18.00 | 97 | 152 | 38.4 | 12 | 99 |
| 18.30 | 85 | 139 | 38.8 | 14 | 99 |
| 19.00 | 90 | 154 | 39.1 | 14 | 98 |
| 19.30 | 88 | 211 | 39.6 | 14 | 98 |
| 20.00 | 72 | 226 | 39.4 | 14 | 98 |
| 20.30 | 97 | 204 | 39.2 | 14 | 98 |
| 21.00 | 90 | 180 | 38.8 | 14 | 99 |
| 22.00 | 88 | 166 | 39 | 14 | 100 |
| 23.00 | 84 | 171 | 37.8 | 14 | 100 |
| 00.00 | 85 | 104 | 37.4 | 14 | 100 |
| 01.00 | 99 | 90 | 37.1 | 14 | 100 |

Abbreviation: MAP (mean arterial pressure), HR (heart rate), T (temperature), RR (respiration rate), SpO2 (peripheral oxygen saturation)

Table 3. Thyroid function

| | Day 0 | Day +1 | Day +2 |
|---|---|---|---|
| TSHs (uIU/mL) | <0.05 | 0.19 | 0.02 |
| fT4 (pmol/L) | 25.4 | 44.43 | 35.79 |
| T3 (nmol/L) | 3.33 | 4.62 | 3.71 |

Table 4. Surgeries Commonly Associated with Postoperative Pulmonary Hypertension

| |
|---|
| Transplantation |
| Heart: follows chronic heart failure |
| Lung: especially if done for pulmonary hypertension |
| Liver: preoperative portopulmonary hypertension |
| Kidney: long-term (>2 y) hemodialysis |
| Cardiac |
| Valve repair/replacement |
| Mitral most common |
| Aortic less often |
| Congenital heart |
| Congenital intracardiac shunts (ventricular septal defect more than atrial septal defect) |
| Left-ventricular-assist devices |
| Lung resection |
| Pneumonectomy more than lobectomy |
| Thromboendarterectomy |
| Chronic thromboembolic pulmonary hypertension |

## DISCUSSION

TS is a rare but life-threatening complication of thyrotoxicosis that in this case was precipitated by cardiac surgery.[8, 9, 13] TS is characterized by fever or hyperthermia, altered mental status (delerium), gastrointestinal dysfunction, cardiovascular symptoms in particular tachycardia or atrial fibrillation, and high-output cardiac failure.[9, 11]

In this report, we have described a case of TS after MVR in a male patient with a known history of thyroid disease, in which to our knowledge, this was the first case report of a patient with TS after MVR surgery. Dhillon A et al reported a consimilar case of a patient after coronary artery bypass graft (CABG) surgery with TS.[13] In line with our case, they had their patient could not be extubated post-operatively and had persistent fever, tachycardia and altered mental status. Initial work up for fever and altered mental status was unremarkable. He was treated with broad spectrum antibiotics and beta blockers but remained intubated, febrile, and altered mental status. They could find the hint after they performed thyroid function tests around second week of hospitalization that revealed TSH < 0.03 µU/ml, fT4 > 4.5 ng/dl, T3 411.9 ng/dl and thyroid stimulating immunoglobulin 269%. They could treat the patient subsequently.[13]

TS was diagnosed according to the Burch–Wartofsky criteria. This set of diagnostic criteria assessed the likelihood of TS by scoring clinical features such as body temperature, central nervous system effects, gastrointestinal or hepatic dysfunction, heart rate, heart failure, atrial fibrillation, and precipitant history. The scale ranges from 0 to 140 points, in which a score greater than 60 is highly compatible with thyroid storm. The score in this patient was 75 points which was reffered as highly suggestive for thyroid storm. The final diagnosis was based not only on this clinical score but also on thyroid function tests and response to therapy.

TS should be distinguished from other causes of hypermetabolic postoperative states, such as sepsis, malignant hyperthermia, and neuroleptic malignant syndrome. The recognized triggers for thyroid storm include trauma, pregnancy, and infection. It was likely that the trauma of cardiac surgery triggered the thyroid storm in this patient.

Standard therapy for TS is multimodal like an antithyroid, beta-blocker, iodine, and glucocorticoid.[3] Initial treatment with antithyroid agent such as propylthiouracil (PTU) and methimazole. Propylthiouracil inhibits the synthesis of thyroid hormone by blocking the oxidation of iodine in the thyroid gland and blocks synthesis of T4 and T3. Iodine therapy suppresses the release of thyroid hormone through the Wolff–Chaikoff effect. Hydrocortisone therapy blocks peripheral conversion of thyroxine to triiodothyronine. Beta-blocker was aimed to control symptoms. In hemodynamically stable patients, beta-blocker is useful to counteract the increased adrenergic tone observed in thyroid storm.[8, 10, 12]

In our case, we administered antithyroid propylthiouracil 200 mg every 4 hours, non-selective beta-blocker propanolol 80 mg every 8 hour, hydrocortisone 100 mg every 8 hours, and lugol 8 drops every 6 hours were administered. Patient was still supported by mechanical ventilation until 24 hours recovery from TS. Patient was extubated in the ICU at 72 hours postoperatively.

In line with our case, Dhillon A et al reported that their patient was administered with stress doses of steroids, propylthiouracil and continued on beta blocker.[13] He was started on hydrocortisone 100 mg every 8 hours, propylthiouracil 100 mg every 8 hours and continued on beta blocker, titrated to heart rate. Over next 72 hours his heart rate, fever and mental status improved and he was successfully extubated. He was discharged on oral methimazole and tapering dose of steroids.[13]

In rare cases, patients may develop more severe allergic reactions and need to discontinue medical management. In these circumstances, treatment with either surgery or radioactive iodine should be considered.[11] However, anti-thyroid medication worked well in our case without any allergic reaction.

Postoperative PH is a challenging and feared complication of many types of surgery, including lung and heart transplantation, pulmonary thrombo-end-arterectomy, congenital-heart-disease repair, and others. The most severe manifestation is acute right heart syndrome, characterized by right heart failure and cardiovascular collapse that is associated with a high mortality. When PH is known preoperatively, risk factors for postoperative complications can be assessed to aid in deciding whether to proceed with the surgery and how to prepare for potential complications (Table 4).[4, 5, 14]

In our case, preoperative PH was apparently caused by backward failure from rheumatic chronic mitral regurgitation, in which first manifestated as post-capillary PH.[4] However, we could not certain whether hyperthyroidism took place in progressivity of PH in this patient or not.

Patients with postoperative PH must be carefully evaluated to identify reversible contributing factors such as fluid and metabolic imbalance, hypoxemia, and right heart ischemia. A pulmonary arterial catheter and echocardiogram are recommended for evaluation, although their value has not been established in carefully designed trials. Management of postoperative PH depends on its severity and the results of careful evaluation.[4, 14] Hence, within close monitoring, our patient in this case did not experience pulmonary hypertensive crisis.

The post-operative period represents a high-risk time for PH patients. Basic management for stabilizing hemodynamic in PH include: maintenance of systemic perfusion pressure (systemic vascular resistance, SVR), optimization of cardiac inotropy (myocardial contractility, preload, and sinus rhythm, if possible), and avoidance of elevations in pulmonary vascular resistance (PVR) by using lung-protective ventilator strategies and reducing right-ventricular afterload using pulmonary vasodilators, and avoidance of myocardial depressants. If a patient has mild to moderate PH, we should perform the preservation of right-heart function, and is otherwise clinically stable, then PH can merely be observed, assuming fluid and metabolic status, left-side filling pressure, and systemic blood pressure is optimized.[14]

Unfortunately, controlled trials upon which to base therapy are lacking, and most approaches are supported only by uncontrolled or anecdotal evidence. Better understanding of the pathophysiology of right heart failure and controlled trials testing therapeutic approaches are needed if we are to make progress in treating this heretofore highly mortal condition.[4, 14]

## CONCLUSION

Thyroid storm after MVR surgery was an important rare case and life-threatening. The post-operative period represented a high-risk time for patients with PH and TS. Survival of TS can only be optimized by early diagnosis and prompt initiation of multimodal therapy including supportive measures and treatment of the precipitating event. Patients with TS and PH should be managed and monitored in an intensive care setting in the first few days following surgery as there was a high risk for mortality and morbidity.

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