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CASE REPORT

INTERMEDIATE

HEART CARE TEAM/MULTIDISCIPLINARY TEAM LIVE

A "Grave" Case of Mitral Regurgitation

Cardio-Obstetric Approach to Severe Mitral Regurgitation With Cardiogenic Shock

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ABSTRACT

A 26-year-old woman presented at 26 weeks of pregnancy with severe mitral regurgitation (MR) and cardiogenic shock in the setting of profound hyperthyroidism. An intra-aortic balloon pump was placed, and surgical intervention was considered. However, with management of thyrotoxicosis and delivery, complete resolution of MR and cardiogenic shock was achieved. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2022;4:1227-1230) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 26-year-old woman at 26 weeks of pregnancy was admitted with a 1-week history of dyspnea, cough, and diarrhea. She was afebrile, with blood pressure of 153/59 mm Hg, heart rate of 88 beats/min, and oxygen saturation of 98% on room air. Physical examination was notable for a symmetrically enlarged thyroid, bilateral rales, elevated jugular venous pressure, a grade III holosystolic murmur at the apex, 2+ bilateral lower extremity edema, warm skin, and extension tremor. Laboratory studies demonstrated significant thyrotoxicosis. An obstetric sonogram revealed a singleton gestation, at 26 weeks and 5 days, with a fetal weight of 1,034 g. The biophysical score was 8/8, the mean vertical pocket of fluid was 4.5 cm, and total amniotic fluid index was 13.4 cm. The fetal heart rate was normal, at 140 beats/min. The fetus was in breech presentation, with a posterior placenta.

LEARNING OBJECTIVES

- To understand the cardiovascular effects of toxic Graves disease and the clinical course of severe MR secondary to a thyrotoxic state.
- To recognize the unique challenges of managing severe valvular regurgitation in the pregnant patient.

Maternal Graves disease had been diagnosed 7 months earlier and treated with methimazole and propranolol. The patient received inconsistent prenatal care and had discontinued medications at 9 weeks of gestation out of self-identified concern for teratogenicity. Her obstetric history is significant for 2 previous cesarean deliveries. The first was for arrest of descent in 2017 at full term, and the second was in 2021 for preterm labor, with 33-week diamniotic dichorionic twin gestation delivered by elective repeat cesarean birth. A routine transthoracic

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ABBREVIATIONS AND ACRONYMS

IABP = intra-aortic balloon pump

ICU = intensive care unit

LV = left ventricular

MR = mitral regurgitation

TEE = transesophageal echocardiogram

TTE = transthoracic echocardiogram

T_3 = triiodothyronine

T_4 = thyroxine

echocardiogram (TTE) performed during her previous pregnancy 3 years earlier was normal.

QUESTION 1: WHAT IS THE DIFFERENTIAL DIAGNOSIS IN OUR PATIENT?

The differential diagnosis included thyrotoxicosis, previously undiagnosed cardiomyopathy, valvular heart disease, or acute preeclampsia.

QUESTION 2: WHAT INVESTIGATIONS ARE NEEDED AT THIS STAGE?

An electrocardiogram demonstrated normal sinus rhythm. Laboratory evaluation revealed normal kidney function without proteinuria. The thyroid profile showed the following: thyroid-stimulating hormone, <0.002 mU/L (0.35-4.70 mU/L); free thyroxine (T_4), 3.3 ng/dL (0.7-1.9 ng/dL); total triiodothyronine (T_3), 358.7 ng/dL (79-149 ng/dL); and thyroid-stimulating immunoglobulin, 13.90 IU/L (<0.56 IU/L). TTE demonstrated normal left ventricular (LV) size and systolic function, with an ejection fraction of 60%. The mitral valve had a restricted posterior leaflet resulting in an eccentric posteriorly directed jet of severe mitral regurgitation (MR) (Video 1). The estimated pulmonary artery systolic pressure was 72 mm Hg, and the inferior vena cava was dilated, with abnormal respiratory collapse.

QUESTION 3: WHAT IS THE IMMEDIATE MANAGEMENT PLAN?

Intravenous diuretic agents and antihypertensive medications were introduced to decrease congestion and reduce myocardial afterload. All vasoactive medications were carefully titrated to avoid compromising placental perfusion. The patient's hyperthyroidism was treated with methimazole, propranolol, and cholestyramine. Iodine was discontinued out of concern for effects on the fetal thyroid. Betamethasone was administered to promote fetal lung development.

The origin of the severe MR was not certain, and the differential diagnosis included previously undiagnosed structural valvular disease and MR secondary to thyrotoxicosis, which has been previously described in the literature.[1,2] A more definitive evaluation of the valve morphology with a transesophageal echocardiogram (TEE) once the patient had undergone diuresis and was euvolemic was planned.

TABLE 1 Right-Sided Heart Catheterization Data

End-expiratory pressure, mm Hg	
Right atrium, mean	26
Pulmonary artery	42/33; mean 36
Pulmonary capillary wedge	23; V-wave −40
Saturation, %	
Pulmonary arterial	74
Systemic arterial	98
Outputs	
Fick cardiac output, L/min	8
Fick cardiac index, L/min/m^2	4.6
Hemoglobin, g/dL	8.5

On hospital day 3, despite attempts at afterload reduction and diuresis, the patient developed cardiogenic shock, with pulmonary edema, hypoxia, and end-organ hypoperfusion with lactic acidosis (Society for Cardiovascular Angiography and Interventions cardiogenic shock stage C).[3]

QUESTION 4: WHAT ARE THE NEXT STEPS IN THE MANAGEMENT OF CARDIOGENIC SHOCK IN A PREGNANT WOMAN WITH SEVERE MITRAL REGURGITATION?

She was transferred to the cardiac intensive care unit (ICU). A multidisciplinary team involving heart failure and interventional cardiology, cardiothoracic surgery, endocrinology, maternal-fetal medicine, and cardiac anesthesiology was assembled to optimize the care of the patient and the fetus. Mechanical ventilatory support was initiated, and an intra-aortic balloon pump (IABP) was inserted without fluoroscopic guidance to avoid radiation to the fetus. Diuresis and antihypertensive medications were uptitrated, with rapid improvement in pulmonary edema, but progressive oliguric renal failure developed. Pulmonary artery catheterization revealed elevated filling pressures with biventricular dysfunction (Table 1). Continuous venovenous hemodialysis was initiated, and with normalization of cardiac filling pressures, there was improvement in her renal function and urine output. Fetal monitoring was performed routinely with biophysical profiles. The nonstress test result was minimally reactive but without fetal heart rate decelerations, deemed secondary to maternal sedation. The patient was extubated on hospital day 5.

Shortly thereafter, there was a nonreassuring fetal biophysical profile of 2 out of 10 and a category III fetal nonstress test result, with further concern for placental abruption on sonogram. Therefore, an emergency cesarean delivery was performed, with

confirmation of placental abruption. This procedure was done through a multidisciplinary approach involving cardiology, maternal-fetal medicine, neonatal ICU, obstetric and cardiothoracic anesthesiology and using IABP support with continuous hemodynamic monitoring.

QUESTION 5: WHAT ARE THE ANTICIPATED HEMODYNAMIC CHANGES DURING PREGNANCY, AND HOW DO THEY AFFECT VALVULAR REGURGITATION?

Hemodynamic changes during pregnancy itself also affect valvular regurgitation.[4] Although MR is generally well tolerated in pregnancy, the impact of pregnancy on this condition is highly variable and can change throughout pregnancy. Pregnancy is a volume-overloaded state that can result in physiologic chamber dilatation and worsening of valvular regurgitation. However, decreased systemic vascular resistance results in reduced LV afterload, which may be beneficial in the setting of MR. Immediately postpartum, venous return to the heart increases, and triggers such as pain and uterine compression of the vasculature can increase afterload and exacerbate valvular disease.[1] Therefore, meticulous management of hemodynamics during and immediately following delivery is essential. Our patient remained hemodynamically stable throughout the procedure.

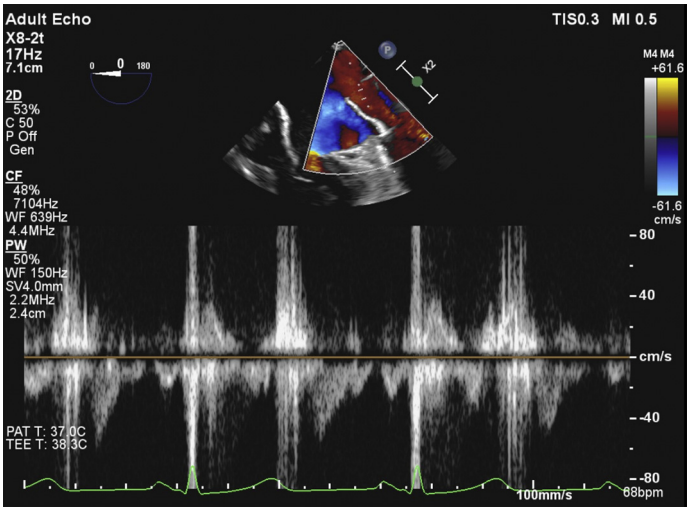
Further, in our patient, delivery had an overall salutary effect on the MR. A male infant was delivered in breech presentation by vertical uterine incision, and he weighed 1,090 g. The infant was noted to have an Apgar score of 5 at 1 minute and 8 at 5 minutes, but because of persistent respiratory distress, he was intubated at 5 minutes of life and admitted to the neonatal ICU. A thyroid profile performed on neonatal day 1 revealed evidence of hypothyroidism, and the baby was initiated on thyroid replacement therapy.

By hospital day 6, maternal euthyroid status (free T_4, 1.5 ng/dL; free T_3, 3.3 pg/mL) had been achieved. However, a TEE revealed persistent severe MR despite IABP support (**Figure 1,** Video 2), with tethering of the posterior mitral leaflet.

QUESTION 6: WHAT IS THE PATHOPHYSIOLOGY OF MITRAL REGURGITATION IN THYROTOXICOSIS?

MR secondary to thyrotoxicosis is thought to be a result of the following: 1) impaired collagen metabolism and accumulation of glycosaminoglycans resulting in myxomatous changes in the leaflets, chordal degeneration, and papillary muscle dysfunction (primary valve dysfunction)[2,5]; and 2) a high-output state resulting in LV enlargement and annular dilatation (secondary valve dysfunction).[2,6] Previous reports with histopathologic examination of harvested valves demonstrated disorganized fragmentation, tear of collagen, and elastin fibers with myxomatous changes.[5,7] In our case, the MR was caused by posterior leaflet tethering, likely secondary to papillary muscle dysfunction.

FIGURE 1 **Pulmonary Vein Flow Reversal on Transesophageal Echocardiogram Suggestive of Severe Mitral Regurgitation.**



QUESTION 7: HOW IS SEVERE MITRAL REGURGITATION SECONDARY TO HYPERTHYROIDISM MANAGED?

There are previous reports of thyrotoxicosis complicated by valvular heart disease with improvement after achieving a euthyroid state.[6,8,9] However, no previously reported cases included severe MR resulting in cardiogenic shock requiring mechanical circulatory support. In our patient, it was unclear whether the MR would improve with medical therapy or would necessitate surgical intervention. The time frame for improvement in MR with antithyroid therapy can be highly variable, from days to as long as 9 months in previous reports.[5,7,10] For patients with chordal rupture, however, definitive surgical intervention has been required.[5,7] A heart team discussion was held regarding the most appropriate treatment of the severe MR. Considering that the MR could improve with resolution of the thyrotoxicosis and the absence of chordal rupture, surgical intervention was deferred.

A TTE performed on day 14, with the IABP on standby, demonstrated improvement in MR severity (Video 3), and the IABP was successfully removed. On day 16, a TTE showed only mild MR (Video 4). Further, a cardiac magnetic resonance scan performed on hospital day 17 demonstrated complete resolution of MR (Video 5). The patient remained asymptomatic and was discharged home. The infant was recovering well in the neonatal ICU but has remained hypothyroid, requiring thyroid hormone replacement.

CLINICAL PERSPECTIVES

This case demonstrates the complexity of managing maternal cardiovascular disease from severe MR secondary to thyrotoxicosis resulting in cardiogenic shock. The importance of using a multidisciplinary approach, with consideration of both maternal and fetal health, and the physiologic changes that occur with pregnancy and the postpartum period, cannot be overstated. In our patient, with treatment of hyperthyroidism and management of the pregnancy state, there was complete resolution of MR and cardiogenic shock.

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KEY WORDS cardiogenic shock, hyperthyroidism, Graves disease, mitral regurgitation, pregnancy

APPENDIX For supplemental videos, please see the online version of this article.

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