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Case Report

Successful Management and Risk Stratification by Exercise Right Heart Catheterization Before Pregnancy in a Patient With Pulmonary Arterial Hypertension

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Despite recent advancements in pharmacologic treatment, guidelines for patients with pulmonary arterial hypertension (PAH) recommend discussion about maternal risks, and they recommend offering pregnancy termination if pregnancy occurs. Preconceptional risk stratification and its association with pregnancy outcomes in women with PAH should be prospectively studied. We present the case of a patient with idiopathic PAH (IPAH) who was risk-stratified using an exercise stress test before pregnancy.

Case Presentation

A 40-year-old woman (gravida 3, para 0, two spontaneous miscarriages at 33 years of age) was diagnosed with IPAH at age 34 years. Right heart catheterization (RHC) at the time of diagnosis revealed pulmonary artery pressure of 79/24 mm Hg, mean pulmonary artery pressure (mPAP) of 50 mm Hg, pulmonary vascular resistance (PVR) of 11.7 Wood units, and cardiac output (CO) of 3.9 L/min calculated using the Fick method. We administered PAH-targeted drugs, including tadalafil and ambrisentan. Due to side effects, ambrisentan was replaced with bosentan, which was subsequently replaced with macitentan, with the expectation of further hemodynamic improvement (Fig. 1). RHC revealed no improvement in hemodynamics by 4 months of treatment (mPAP of 44 mm Hg; PVR of 8.2 Wood units; right atrium pressure (RAP) of 8 mm Hg; CO of 4.3 L/min; World Health Organization functional class [WHO-FC] III). Therefore, intravenous epoprostenol was initiated and titrated up to 115 ng/kg/min over 12 months, leading to hemodynamic improvement (mPAP of 21 mm Hg; PVR of 2.2 Wood units; RAP of 4 mmHg; CO of 4.8 L/min; WHO-FC I). When the patient was aged 37 years, intravenous epoprostenol was transitioned to subcutaneous treprostinil, due to repeated catheter infections. Thereafter, her hemodynamics at rest were stable, and exercise RHC was performed to examine the feasibility of switching from treprostinil to oral selexipag. No exercise pulmonary hypertension was confirmed by exercise stress RHC (mPAP of 28 mm Hg during 10.0 L/min of CO at peak exercise; mPAP-CO slope of 2.6; peak Work Rate of 70 Watts; resting heart rate (HR) of 74 beats per minute; and peak HR of 124 beats per minute). These results suggested that switching from treprostinil to oral selexipag was feasible, based on the criterion that the parenteral prostacyclin can be safely tapered with the aid of an exercise RHC, as previously reported by our hospital (Supplemental Methods).[1]

The patient reported her decision to become pregnant, and we respected her decision, even though we had considered switching from treprostinil to oral selexipag. We informed the patient and her family about the risks of deterioration of PAH at any time during or after pregnancy, to aid her in making informed decisions. Taking into consideration these clinical courses, alongside exercise stress RHC data, we respected the patient's decision to get pregnant. Macitentan was discontinued due to teratogenicity. Six months later, the patient became pregnant. Based on the decision of a multidisciplinary team of cardiologists, obstetricians, gynecologists, and anesthesiologists, oral tadalafil and subcutaneous treprostinil were continued during pregnancy. Prophylactic or therapeutic anticoagulation was not used. Regular monthly outpatient clinic visits revealed no abnormalities in symptoms, physical examination, plasma brain natriuretic peptide level, or electrocardiography. The plasma brain natriuretic peptide values remained under 20 pg/mL during pregnancy and delivery. No deterioration of the right heart parameters was seen when echocardiography

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Ethics Statement: The patient provided informed consent for the preparation of this report.

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Novel Teaching Points

- The apparent key to the successful management of PAH in pregnancy is a multidisciplinary team approach, including the preconceptional assessment of pulmonary vascular reserve, pharmacologic management, close management of heart failure, and careful delivery timing.
- Exercise stress testing may be helpful in preconceptional risk assessment in patients with PAH.

was performed (e.g, estimated right ventricular systolic pressure 38 mm Hg; tricuspid annular plane systolic excursion 30 mm; estimated RAP 0∼5 mm Hg). We evaluated RHC in the 32nd week of pregnancy (when the patient was in the third trimester, at age 40 years), when pregnancy-associated fluid retention became pronounced and the risk of radiation exposure to the fetus was reduced. RHC showed an mPAP of 22 mm Hg, PVR of 2.9 Wood units, RAP of 3 mm Hg, and CO of 5.1 L/min. Four days before delivery, intravenous heparin was administered. We performed an elective cesarean section under spinal anesthesia in the 38th week, according to the schedules of the multidisciplinary team. She delivered a healthy boy weighing 2211 g, with 1-minute and 5-minute Apgar scores of 8 and 9 points, respectively, in an operating room with hemodynamic monitoring. After delivery, the patient spent 2 days in the intensive care unit, for close monitoring and volume adjustment. The postpartum period was uneventful. RHC was performed at 9 months after delivery (mPAP of 20 mm Hg; PVR of 4.6 Wood units; RAP of 4 mm Hg; and CO of 2.9 L/min) without any change of PAH medications. No derioration occurred in right heart failure or functional class (ie, WHO-FC I was maintained).

Discussion

A retrospective study with exercise stress RHC was used to help in pregnancy planning for this patient with PAH.

Exercise stress test for preconceptional risk stratification

Exercise stress RHC showed no exercise pulmonary hypertension, indicating mild pulmonary vasculopathy. Therefore, we felt that the level of risk with pregnancy was acceptable because pulmonary circulation could withstand the increased CO during the perinatal period. No exacerbation of mPAP or PVR was observed during the increase in CO. At the 20th-24th weeks of gestation, CO increases by 30%−50% and it is maintained at a similar level throughout pregnancy because of increased blood volume, increased HR, and reduced systemic vascular resistance, which leads to lower afterload. The right ventricle is overloaded during the third trimester of pregnancy because of cardiovascular stress brought on by a volume shift. The risk of cardiac events, such as right heart failure, is higher during the third trimester of pregnancy, at delivery, and postpartum. Pregnancy is life's cardiovascular stress test.[2] A preconception exercise stress test has been recommended to identify those patients with congenital heart disease who are at elevated risk for cardiac complications.[3,4] A reason for this recommendation might be that the exercise stress test can simulatethe increase in CO observed during late pregnancy, to confirm the pulmonary vascular response. The normal pulmonary vascular bed is a low-pressure, low-resistance, highly distensible system that can adapt to large increases in blood flow, such as that during physical exercise, with minimal elevation of pulmonary artery pressure. Exercise pulmonary hypertension may be indicative

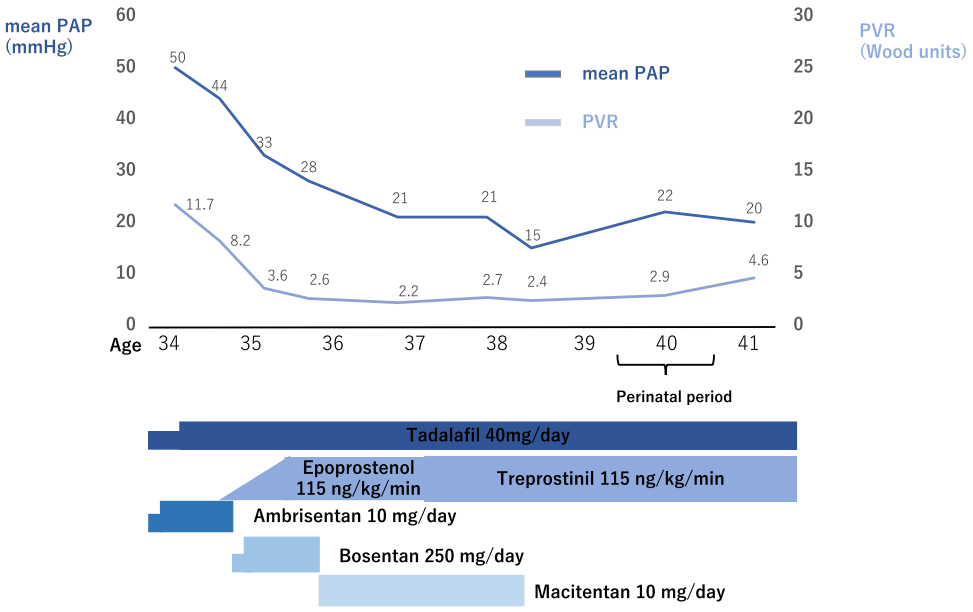

Figure 1. Clinical course from initial treatment to after childbirth. PAP, pulmonary artery pressure; PVR, pulmonary vascular resistance.

of an advanced degree of pulmonary vasculopathy and progressive remodeling, which is a decrease in pulmonary vascular reserve.[5]

Pregnancies with PAH continue to have high maternal mortality rates (11%-25%).[6] Hence, current guidelines continue to discuss maternal risks and offer pregnancy termination if pregnancy occurs, in all patients with PAH. However, recent advancements have improved PAH prognosis and control, allowing an increasing number of young women with PAH to lead nearly normal lives. A recent case series investigating pregnancies in such women evidenced that good outcomes are achievable,[7] especially in patients with well-controlled disease, when managed by a multidisciplinary team.

Management of PAH during pregnancy

European Society of Cardiology/European Respiratory Society guidelines recommend that if a pregnancy is continued, PAH therapy be adjusted as needed for teratogenicity. Furthermore, compared with nonpregnant women, pregnant women with pulmonary hypertension have a risk of venous thromboembolism that is almost 5-fold higher. Therefore, performing a risk assessment is important, to determine whether antithrombotic therapy should be administered to the patient. In our case, the endothelin receptor antagonist was discontinued in consideration of use of treprostinil and phosphodiesterase-5 inhibitors due to potential teratogenicity. In addition, because the patient was not at high risk for thrombosis, antithrombotic therapy was not administered, except at a point shortly before delivery. In addition, attention much be given to the possibilities of premature birth, intrauterine fetal growth retardation, and anomalies.

The apparent key to successful management of PAH in pregnancy is a multidisciplinary team approach, including assessment of pulmonary vascular reserve preconception, pharmacologic management, close management of heart failure, and careful timing of delivery. In the recent era of improved treatment, further accumulation and investigation of cases are expected. Furthermore, prospective international validation of the usefulness of exercise stress testing for preconceptional risk assessment is required.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2023.01.004.