Case Report

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Role of Meticulous Observation: Successful Pregnancy in a 30-Year-Old Woman with Severe Pulmonary Hypertension

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Pregnancy is strongly discouraged in patients with pulmonary arterial hypertension (PAH). Herein, we report a successful delivery in a woman with PAH using a multidisciplinary approach. A 30-year-old pregnant woman with PAH was referred to us with a chief complaint of dyspnea. She was advised to terminate her pregnancy but she refused to do so despite several recommendations by healthcare professionals. She was scheduled for treatment with iloprost (brand name: Ilomedin) and heparin infusions for 3-4 days at 20-day intervals. She spent her last month of pregnancy in a hospital under close observation and received iloprost infusion. She underwent a successful cesarean section under general anesthesia at week 36 of gestation. Iloprost administration was continued for one week after delivery and was changed to bosentan after that. Meanwhile, heparin infusion was substituted by warfarin. However, treatment with bosentan led to a temporary interruption in breastfeeding. A few days later, she presented with severe dyspnea and pulmonary artery pressure of 110 mmHg. Treatment was restarted with iloprost, followed by stabilization with bosentan. A successful delivery was achieved in this situation by meticulous observation and aggressive treatment targeting PAH, along with long-term hospital stay and multidisciplinary management. Severe PAH is regarded as a contraindication to pregnancy. While physicians strongly recommend termination of pregnancy in such patients, some of them might refuse and insist on delivery of the baby. Similar pregnant cases with potential delivery are recommended to be evaluated for effective management of this condition.

Key words: Pulmonary artery hypertension, Pregnancy, Termination

INTRODUCTION

Pulmonary arterial hypertension is defined as a group of diseases characterized by a progressive increase in pulmonary vascular resistance leading to right ventricular (RV) failure and premature death (1). Pulmonary complication is an ominous prognostic sign, mainly observed in patients with collagen vascular diseases (2). However, PAH affects a relatively small number of pregnant women (approximately 0.0003%) (1).

Recent guidelines of the European Society of Cardiology for management of PAH and the statement by the American College of Cardiology/American Heart Association strongly discourage pregnancy in patients with PAH and recommend termination of pregnancy. During the past decade, new advanced therapies for treatment of PAH have been developed, leading to improved overall quality of life and prognosis of these

patients. Moreover, early detection of underlying diseases, improved understanding of cardiopulmonary pathophysiology, enhanced obstetric/anesthetic management and introduction of a multidisciplinary approach have significantly contributed to the management of high-risk pregnancies.

In this report, we discuss the clinical course of a patient with critical PAH at week 18 of gestation and successful delivery by adopting a multidisciplinary approach.

CASE SUMMARY

A 30-year-old pregnant woman was referred with a chief complaint of dyspnea at week 18 of gestation. She presented with PAH due to collagen vascular disease (systemic lupus erythematosus). She had experienced four miscarriages in the first and second trimesters, as well as two elective premature abortions due to uncontrolled medical condition. On admission, she was hemodynamically stable with proper functional class. Afterwards, she was treated with warfarin, prednisolone, and hydroxychloroquine. Her physical examination was unremarkable, with an exception of II/VI systolic murmur auscultated at the left sternal border.

Her electrocardiogram revealed RV hypertrophy, while echocardiogram indicated a mild tricuspid regurgitation and severe PAH (Figure 1). The left ventricle was normal, and the estimated systolic pulmonary artery pressure (PAP) was 60 mmHg. A previous cardiac catheterization demonstrated a PAP of 80/28 (mean 47 mmHg) with negative adenosine stress test. The six-minute walking test was 500 m and she had a tricuspid annular plane systolic excursion (TAPSE) of 22 cm supporting normal RV function.

The routine biochemical parameters were within the normal range, with the exception of mild anemia. Moreover, she was positive for anti-dsDNA and lupus anticoagulant tests. Our patient refused to terminate her pregnancy despite several recommendations by healthcare professionals. Therefore, after considerable discussion, she agreed to receive 5 ng/kg/min of iloprost (Ilomedin) and heparin infusion for 3-4 days for a 20-day interval. Thereafter, monthly follow-ups consisted of 6MWT and measurement of PAP, TAPSE, NT-proBNP levels, and RV function. Uncharacteristically, the results indicated no significant change in the indices during the entire course of management. She spent the last month of her pregnancy in a hospital under close observation and received iloprost infusion during her admission.

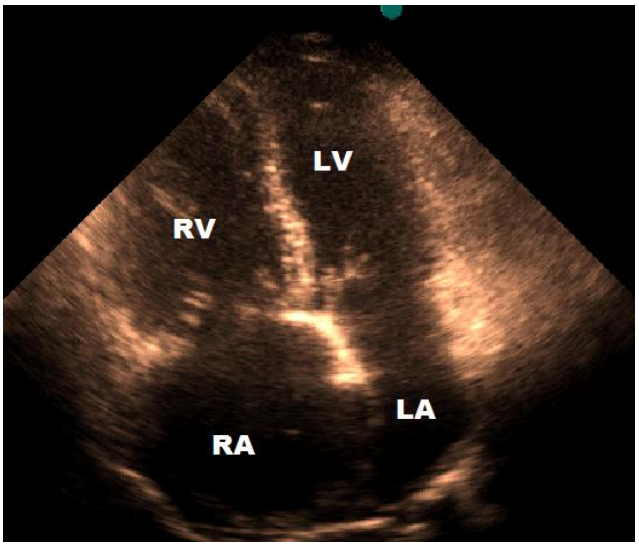

Figure 1. Trans-thoracic echocardiography demonstrates RV hypertrophy and enlargement of both right atrium and ventricle.

Eventually, the patient underwent a successful cesarean section under general anesthesia at week 36 of gestation. Administration of iloprost continued one week postpartum and was substituted by bosentan; meanwhile, heparin was replaced with warfarin. Treatment with bosentan led to a temporary interruption in breastfeeding. A few days later, she was referred with severe dyspnea. Echocardiography results revealed severe RV enlargement and dysfunction with severe PAH (PAP of 110 mmHg). Treatment was restarted with iloprost, and the patient was stabilized and discharged on bosentan. At discharge time, the PAP was about 55 mmHg. In summary, a successful delivery was achieved by meticulous observation and aggressive treatment targeting PAH with long-term hospital stay and multidisciplinary management.

DISCUSSION

Before 1985, median survival of PAH was 2.8 years after diagnosis, with no known effective therapy (3). Epoprostenol was the first medicine approved for this condition in 1996, and significant advances have occurred in treatment of such cases ever since, including the addition of many novel PAH specific medical therapies, which improve management of symptoms and survival rate (4). Despite such improvements, previous case studies have reported maternal mortality rate of pregnant PAH patients to be 30%-56%, with premature delivery occurring in more than 50% of patients and the highest risk of accelerated mortality, not during delivery but uncharacteristically afterwards in the first 10 days postpartum (5).

Maternal mortality rate is associated with increased demand on the cardiopulmonary system during pregnancy. Physiologic events place a great demand on the cardiovascular system, with the greatest incidence of mortality occurring during the first several postoperative days presumably due to high degree of fluid shifts and the labile afterload state.

Pregnancy to full-term is allowed in women with mild PAH and normal cardiac function. Pregnancy to 32 weeks under intensive care and delivery through cesarean section are tolerable in cases with moderate PAH, but termination of pregnancy is advised to cases with severe PAH (6). But gradually, the outcome of pregnancy in patients with PAH has improved. This advance could be attributed to the wide application of several classes of substances in tailored approaches (7). In the recent years, advanced therapies (prostacyclin analogues, phosphodiesterase inhibitors, and endothelin-receptor antagonists) have revolutionized PAH management. Prostacyclin is predominantly produced in endothelial cells leading to induced potent vasodilatation of all vascular beds. In addition, it is the most effective endogenous inhibitor of platelet aggregation and has both cyto-protective and anti-proliferative roles (8, 9). Epoprostenol (synthetic prostacyclin) improves exercise capacity and pulmonary hemodynamics as well as symptoms in both clinical conditions. Moreover, this substance is the only treatment associated with improved survival in PAH in a randomized study (10). Therefore, we used iloprost for several weeks prior to the expected date of delivery in order to maximize its benefits. Iloprost therapy was continued after the delivery considering the increased incidence of postpartum complications.

Bosentan is the first orally active dual endothelin-A and endothelin-B receptor antagonist, which improves exercise capacity, pulmonary hemodynamics and echocardiographic variables. In addition, a delay in clinical worsening in patients with PAH is observed with bosentan; however, this medicine is contraindicated in pregnancy (11).

CGMP-specific phosphodiesterase type 5 (PDE5) inhibitors lead to prolonged pulmonary vasodilator action of inhaled nitric oxide. This group of inhibitors enhances pulmonary hemodynamics and exercise capacity in patients with PAH and contributes to significant improvement in hemodynamics and six-minute walking test. Nevertheless, the effect of sildenafil on patients with other types of PAH is uncertain.

Advanced PAH therapy and effective thromboprophylaxis must be considered before decompensating of patients or occurrence of thrombotic complications. Maternal safety and well-being need to be weighed against premature delivery, intrauterine growth retardation, and the need for neonatal care when deciding about timing and type of delivery for a patient. Careful monitoring of arterial oxygen saturation, cardiac rhythm, and blood pressure must be carried out for PAH patients in the peripartum period. Safety of the fetus exposed to PAH target treatments is another healthcare concern. Intravenous epoprostenol is reported to be safe during pregnancy. In this case, iloprost caused no fetal deformities or growth retardation.

The use of a "treat-to-target" strategy with frequent visits during pregnancy is recommended for these patients. In addition, patients must be admitted during the third trimester and a multidisciplinary approach should be used

to facilitate management and achieve safe delivery. Detailed plans must be designed (e.g., timing and mode of delivery) and should be accompanied by extensive patient dialogue along with their consent as well as communication with local healthcare professionals prior to delivery (12).

The optimal mode of delivery (cesarean section versus vaginal delivery) in patients with PAH remains a matter of debate. Urgent delivery (e.g., caesarean section) might be needed in cases of maternal hemodynamic deterioration or fetal distress. Close surveillance of fetus and a lower threshold for intervention with early signs of maternal or fetal distress were the main reasons for selecting cesarean section for our patient.

An important component in successful management of these patients involves a multidisciplinary approach with a meticulous observation of patients during pregnancy.

Conflicts of interest

Authors declare no conflicts of interest.

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