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Pregnant Patient with Primary Pulmonary Hypertension: Inhaled Pulmonary Vasodilators and Epidural Anesthesia for Cesarean Delivery

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PRIMARY pulmonary hypertension (PPH) is rarely encountered in pregnant women, but carries a high risk of maternal morbidity and mortality.[1] We report a case of PPH in a pregnant patient treated with antithrombotic drugs, inhaled pulmonary vasodilators, and epidural anesthesia for cesarean delivery; follow-up examination occurred at 6 months.

Case Report

Two years previously, the 26-yr-old woman was diagnosed with PPH after cardiac decompensation, which occurred 5 months after uncomplicated delivery of a neonate. She refused treatment at that time. During her second pregnancy, at 15 weeks' gestation, Doppler echocardiography showed a right atrial diameter of 6.2 cm (normal diameter, 2.2–4.1 cm), a short-axis end-diastolic diameter of the right ventricle of 5.1 cm (normal, 1.9–4.0 cm), a right ventricle with eccentric hypertrophy and fractional area shortening of 33%, and a small, normally contracting left ventricle.

The patient was lost to further follow-up examinations and reappeared at 31 weeks' gestation, severely dyspneic at rest and with dilated neck veins and lower limb edema. Ultrasonograph showed a growth-retarded fetus. The patient's systemic arterial pressure (AP) was 108/69 mmHg, with a regular heart rate of 94 beats/min. Electrocardiography showed a sinus rhythm, prominent P waves in V_1–V_3, and a partial right bundle branch block. Oxygen saturation by pulse oximetry (Sp_{O_2}) of 88% increased to more than 94% with supplemented nasal oxygen. Hemoglobin was 11.4 g/dl, and platelet count was 177 $10^{3\circ}/\mu l$. Radial artery and thermodilution pulmonary artery catheters were inserted to test the response to nitric oxide (NO) and to oxygen breathing at inspiratory fraction (FI_{O_2}) of 1.0. Nitric oxide (40 ppm) failed to improve pulmonary hemodynamics, but oxygen breathing slightly decreased pulmonary artery pressure (PAP) and pulmonary vascular resistance (PVR) and the catheters were removed. Dalteparin (Fragmin; Pharmacia-Upjohn, Stockholm, Sweden), a low-molecular-weight heparin, was administered subcutaneously at 5,000 and 7,500 IU/day. The patient received digoxin, magnesium for its tocolitic properties, and betamethasone at 31 weeks and 32 weeks of gestation to promote fetal lung maturation. Continued right-sided heart dilatation (atrial diameter = 6.3 cm, end-diastolic ventricular diameter = 5.4 cm) and a decrease of right ventricular fractional area shortening to 25% were found at 32 weeks' gestation. Ultrasound biometry showed insufficient fetal growth, and the decision was made to proceed with cesarean delivery at 34 weeks' gestation.

In the operating room, the patient was placed in a supine position with left uterine displacement. Radial artery, thermodilution pulmonary artery, and lumbar epidural (L2–3) catheters were placed during local anesthesia. After baseline measurements, 6 l/min O_2 by mask increased Sp_{O_2} from 90 to 96%. The hemodynamic parameters, hemoglobin concentration, and platelet count obtained peripartum are summarized in table 1. Thromboelastography (reaction time, 6.0 mm; clot

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formation time, 2.0 mm; maximal amplitude, 76 mm; clot formation rate, 74°) and tests of platelet aggregation (65–86%) showed a coagulation profile typical for hypercoagulability of parturients near term.[2,3] An epidural test dose of 3 ml lidocaine, 2% (60 mg), with 15 μg epinephrine was administered. Epidural anesthesia was induced slowly (70 min) with 300 mg plain lidocaine, 2%, 70 mg bupivacaine 0.5%, and 0.1 mg fentanyl. Epidural block finally spread to T_5; the supine position with left-uterine displacement continued to be tolerated. The patient inhaled 20 μg aerosolized iloprost (Ilomedin; Schering, Berlin) diluted in 2 ml NaCl, 0.9%, for 4 min. A 1,590-g and 40-cm (< tenth percentile) infant was delivered by low transverse abdominal incision. Apgar scores were 7, 9, and 9 at 1, 5, and 10 min, respectively. Oxytocin was administered in the uterine wall and as a slow intravenous infusion. Tubal ligation was performed. Unfractioned heparin 5,000 IU was then administered subcutaneously. The patient received 2,400 ml lactated Ringer's solution. Urine volume was 200 ml, and surgical blood loss was 400 ml. Coagulation tests after iloprost inhalation and delivery showed mild changes of reaction time (3.5–4.0 mm), clot formation time (2.0–2.5 mm), maximal amplitude (63–66 mm), clot formation rate (74–76°), and platelet aggregation (65–86%). The epidural catheter remained *in situ*.

In the intensive care unit, continuous oxygen by mask and intermittent iloprost inhalations six times daily were continued. Cardiac output decreased during the first 12 h to 5.4 l/min, and then ranged between 4.1 and 6.4 l/min. Systolic PAP (82–95 mmHg) remained initially below systolic AP, but in the further course exceeded intermittently the AP level without clinical consequences. Systemic vascular resistance (SVR) increased from 567 to 1,180 dyn · s^{-1} · cm^{-5}, and PVR increased from 395 to 890 dyn · s^{-1} · cm^{-5}. Positive fluid balance of 1,600 ml was reduced to 600 ml with furosemide. Postoperative analgesia was provided with intravenous paracetamol and morphine. Thromboelastographic and platelet aggregation tests remained unchanged postpartum, and the epidural catheter was removed 28 h after insertion (25 h after the last heparin dose). Subcutaneous dalteparin administration, 5,000 IU twice daily, was resumed 2 h later. On postpartum day 2, the pulmonary artery catheter was removed. Oral anticoagulation was started on postpartum day 8, and dalteparin was discontinued on postpartum day 10. Home treatment with inhaled iloprost and evaluation for lung transplantation were considered, but the patient's understanding of and potential compliance with the treatment were considered to be inadequate. She was discharged on postpartum day 21, receiving coumarin and digoxin. The newborn required continuous positive airway pressure for 5 days, then recovered and progressed uneventfully.

After discharge, the patient discontinued her medication, became severely dyspneic and cyanotic, and was readmitted to the hospital 1 month later. Six months after delivery of the infant, the patient's clinical condition was stable. Doppler echocardiography showed an atrial diameter of 7.4 cm, an end-diastolic ventricular diameter of 5.7 cm, a low (20%) fractional area shortening of the right ventricle, and a newly patent foramen ovale with right-to-left shunt.

Discussion

Pregnancy in patients with PPH carries a 30% risk of maternal mortality, as compared with a 30–40% rate in Eisenmenger syndrome, and a more than 50% rate in secondary vascular pulmonary hypertension.[1,4–6] Acute and prolonged treatment with inhaled NO and intravenous and inhaled prostaglandins, such as prostacyclin (PGI_2), improve pulmonary endothelial cell function, abnormal platelet aggregation, right-sided heart hemodynamics, and life expectancy in patients with PPH. Side effects, such as bleeding caused by inhibition of platelet aggregation, predominant decrease of SVR and hypoxemia, and complications associated with the drug-delivery system, occasionally limit the intravenous PGI_2 application. NO treatment may also be complicated by platelet inhibition or methemoglobinemia, formation of toxic nitrate metabolites, and technical requirements for its application.[7–11] Aerosolized PGI_2 and its synthetic analog iloprost are more easily administered, do not affect SVR, and more effectively reduce PAP in patients with pulmonary hypertension, compared with intravenous PGI_2 and inhaled NO.[9,10] The experiences with NO and PGI_2 in pregnant patients are currently limited to a few cases.[1,12–16] A patient with Eisenmenger syndrome was treated successfully with NO peripartum; however, methylene blue was necessary because of severe methemoglobinemia. The patient died when NO was discontinued, despite intravenous infusion of PGI_2.[12] In a case of scleroderma, pulmonary hypertension was unresponsive to NO, and the patient died 9 days after delivery of an infant.[13] However, a woman with human immunodeficiency virus infection and pulmonary hypertension was successfully treated with oxygen and NO for several weeks peripartum.[14] Treatment with intravenous PGI_2 was recommended for 12–15 months before conception in patients with PPH.[15] When PPH was diagnosed during pregnancy, one patient responded favorably to PGI_2 and furosemide, but another failed to respond, and died before delivery of a neonate.[15] Another PPH patient was treated with intravenous PGI_2, but bleeding after operative delivery necessitated gradual change to aerosolized PGI_2; the bleeding ceased and the patient recovered.[16]

The echocardiographic and invasive measurements in our patient showed a severe form of PPH with progressive dilation of the right side of the heart. The diameters of the right atrium and right ventricle far exceeded the values found in healthy parturients at term and postpartum.[17] The patient's response to NO at 31 weeks' gestation was inadequate, but oxygen breathing resulted in some improvement in pulmonary hemodynamics. In the operating room, supplemented oxygen and epidural anesthesia provided a stable cardiovascular condition, with a systolic AP greater than the systolic PAP. Inhaled iloprost decreased PAP before delivery and again in the intensive care unit, when PAP started to exceed AP (table 1). The observed changes in PAP and PVR were

Table 1. Effects of Epidural Anesthesia, Iloprost, and Cesarean Delivery on Hemodynamic Parameters, Hemoglobin, and Platelet Count

Operating Room	Epidural Anesthesia					Intensive Care Unit		
	Baseline	40 min	Iloprost	Start CD	Delivery	After CD	40 min	Iloprost	Day 1
Heart rate (beats/min)	113	112	107	104	103	102	105	105	73
Systolic AP (mmHg)	99	97	104	104	91	88	92	97	105
Mean AP (mmHg)	68	64	70	68	69	63	69	68	66
Diastolic AP (mmHg)	50	52	52	52	55	52	55	55	49
Systolic PAP (mmHg)	101	89	81	85	85	85	94	89	81
Mean PAP (mmHg)	65	62	60	59	57	57	60	58	57
Diastolic PAP (mmHg)	50	39	44	43	37	40	45	42	37
RAP (mmHg)	9	10	10	9	10	8	11	10	10
PCWP (mmHg)	8	15	16	15	14	17	19	20	10
Cardiac output (l/min)	7.31	8.00	7.48	8.00	8.53	7.83	9.05	6.61	4.30
SVR (dyn · s^{-1} · cm^{-5})	646	540	642	590	553	562	513	702	1051
PVR (dyn · s^{-1} · cm^{-5})	546	470	471	440	403	409	362	460	882
DO_2 (ml/min)	1,065	1,232	1,109	1,215	1,253	1,144	1,363	970	
VO_2 (ml/min)	317	342	278	358	357	330	379	221	
ExO_2 (%)	30	28	25	29	28	29	28	23	
Hemoglobin (g/l)	10.3		9.9			9.3		10.6	10.4
Platelet count ($10^3/\mu l$)	137		130			134		151	145

Baseline = 45 min after the epidural test dose; Iloprost = 20 μg inhaled over 4 min; CD = cesarean delivery; AP = systemic arterial pressure; PAP = pulmonary artery pressure; RAP = right atrial pressure; PCWP = pulmonary capillary wedge pressure; SVR = systemic vascular resistance; PVR = pulmonary vascular resistance; DO_2 = oxygen delivery; VO_2 = oxygen consumption; ExO_2 = oxygen extraction rate.

moderate and coinfluenced by other factors (*e.g.*, oxygen, epidural anesthesia, volume infusion, delivery and bleeding, and furosemide), but iloprost may have prevented a further increase of PAP and right-sided heart decompensation peripartum.

The use of antithrombotic drugs in pregnant patients with pulmonary hypertension is controversial because of a low incidence of cases, more frequent reports of bleeding than of thromboembolism, concomitant coagulation defects, and subtle differences between PPH, Eisenmenger syndrome, and other types of secondary pulmonary hypertension.[1,4-6] Gestational hypercoagulability and increased pulmonary thrombogenicity of PPH indicate a thromboembolic prophylaxis peripartum.[1,7,11] Therefore, a low-molecular-weight heparin was administered for 4 weeks peripartum, followed by oral anticoagulation. The major concern of the treatment represented the insertion and removal of the epidural catheter and inhalation of iloprost, with its potential to induce platelet dysfunction and, eventually, epidural hematoma. The mild changes of thromboelastographic parameters and platelet aggregation tests excluded the adverse coagulation effect of iloprost in this patient.

This case report confirms the importance of early hospital admission and individually tailored medical treatment in pregnant PPH patients. The use of antithrombotic drugs and selective pulmonary vasodilators are warranted in late pregnancy and particularly after delivery of an infant, to prevent the pulmonary hypertensive crisis and right-sided heart failure. Inhaled iloprost appears to be a promising option to reduce PAP without compromising platelet function, an important characteristic for patients requiring regional anesthesia.

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Narcolepsy and Anesthesia

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NARCOLEPSY is a sleep disorder characterized by excessive daytime sleepiness, involuntary daytime sleep episodes, disturbed nocturnal sleep, sleep paralysis, and cataplexy (sudden loss of muscle tone without loss of consciousness).[1,2] Its treatment includes stimulants (*e.g.*, amphetamines), tricyclic antidepressants, and behavioral therapy.[3,4] Anesthetic implications include increased sensitivity to anesthetic agents, increased risk of postoperative apneic episodes,[5] and interactions with treatment medications.[6] We report a case in which propofol and nitrous oxide were used to successfully anesthetize a patient with a history of narcolepsy and several episodes of prolonged emergence from inhalation anesthesia.

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Case Report

A 51-yr-old woman required wide local excision of a recurrent right thigh mass during general anesthesia. The patient had a life-long history of sleepiness that worsened during the last 8 yr. Four years previously, she underwent evaluation at a sleep disorder center, which included a Multiple Sleep Latency Test, and was diagnosed with narcolepsy characterized by hypnagogic hallucinations, sleep paralysis, and sleep attacks. Family history was positive for daytime sleepiness, although to a lesser extent. The patient reported facial swelling after taking prochlorperazine, itching with use of penicillin, and hallucinations after morphine administration. She denied alcohol or tobacco use.

The patient underwent vaginal hysterectomy with general anesthesia in 1979, in which her emergence time was approximately 8 h. In 1983, she underwent removal of a right thigh lipoma during general anesthesia; after 30 min general anesthesia, she spent several hours in the postanesthesia care unit (PACU), and awoke 9 h later. In 1988, she underwent bilateral breast reduction with general anesthesia. The surgical procedure was 9 h, and the patient awoke 10 h later. In 1989, after a failed attempt to produce spinal anesthesia, she underwent tumor removal from the right leg during general anesthesia induced with thiopental, gallamine, and succinylcholine. Maintenance consisted of isoflurane and nitrous oxide. The patient also received 20 mg intravenous metoclopramide and 0.625 mg droperidol. She did not