

Case #1 (year 1992):

She was 39 years old, gravida 4, para 2. She had an Idiopathic Pulmonary Arterial Hypertension (PAH) revealed during pregnancy by a New York Heart Association (NYHA) functional class II, a mean Pulmonary Artery Pressure (mPAP) of 54 mmHg and a low cardiac index ($1.5 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$, Web table1). Calcium channel blockers therapy was started and she underwent a cesarean section under general anesthesia at 37 weeks gestation. Channels calcium blockers proved to be ineffective with an increasing dyspnea and a mPAP of 86 mmHg when reassessed two years later. Thus, this treatment was discontinued and an intravenous epoprostenol therapy was begun. Pulmonary hypertension improved slowly thereafter and the patient was back to NYHA class I in June 2004.

Case #2 (year 1992):

She was 30 years old, gravida 1. She had an idiopathic PAH revealed during pregnancy by circulatory collapse at 33 weeks gestation. She was admitted directly in the intensive care unit (of the department of pneumology) where dobutamine, furosemide and epoprostenol were started on the basis of hemodynamic data collected with a Swan Ganz catheter (mPAP was 60 mmHg and cardiac index was $1.8 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$, Web table1). Termination of pregnancy was thus decided and induction of labor was performed under low dose epidural analgesia; she had subsequently a normal vaginal delivery and a live neonate (Web table2). However, the patient condition further deteriorated postpartum and she died 3 months later before heart-lung transplantation could be performed.

Case #3 (year 1996):

She was 22 years old, gravida 1. Idiopathic PAH was diagnosed one year before pregnancy. She was in NYHA functional class III; mPAP was 60 mmHg and cardiac index was $2.5 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$, without response to nitric oxide test. The patient had no medical follow-up thereafter. At 12 weeks gestation, she was hospitalized in the intensive care unit because of circulatory collapse; she died several hours later.

Case #4 (year 2002):

She was 38 years old, gravida 1. Idiopathic PAH was diagnosed 15 years before. She was in NYHA functional class II; mPAP was 60 mmHg with positive response to nitric oxide test. Thus, long-term diltiazem treatment was implemented. This therapy was successful with a return to NYHA class I, a decrease in mPAP to 42 mmHg and a normalization of cardiac index (Web table1). The patient was seen at the department of pneumology each month during pregnancy and remained stable with the same treatment. Scheduled cesarean delivery was performed at 37 weeks gestation under general anesthesia (after failure of epidural anesthesia) and was uncomplicated. Postpartum period was also uneventful.

Case #5 (year 2001):

She was 32 years old, gravida 2. She had had an ectopic pregnancy 8 years before, which had required only a medical therapy. A new pregnancy had been discouraged because of a severe congenital heart disease-associated PAH. She was in NYHA class III; mPAP was 91 mmHg and cardiac index was $3.2 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$. She had nasal oxygen prongs at home plus venesection once a month. Nonetheless, she

became pregnant again and developed a cyanosis along with a deterioration of her echographic cardiac index (Web table1). Cesarean section was thus decided at 32 weeks gestation and performed under low dose combined spinal epidural anesthesia (using 1.25 mg isobaric bupivacaine + 2.5 mcg sufentanil intrathecally, followed by 10 ml of 2% lidocaine with epinephrine 1/600,000). She remained stable during surgery using inhaled nitric oxide and did not deteriorate clinically in the immediate postpartum period despite a high mPAP and a low cardiac index (Web table1). She was still alive and in a stable clinical condition at the one-year postnatal visit (manuscript, table II).

Case #6 & #9 (year 1995 & 2002):

She was 32 years, gravida 2 after an early spontaneous abortion. This patient had a congenital heart disease-associated PAH with an atrial septal defect (ostium primum) and a mitral regurgitation associated with an interventricular septal defect. She was treated with oral digoxin 0.125 mg daily. She remained stable during pregnancy and did not wish to have medical follow-up. She presented in labor at night at 40 weeks gestation. Continuous spinal analgesia was chosen by the attendant anesthesiologist and she had subsequently an uneventful vaginal delivery.

Despite unfavorable medical counseling, she became pregnant again when she was 38 years old. She had a hemoptysis at the beginning of this second pregnancy and another one at 32 weeks gestation; at this time her systolic PAP had increased from 62 to 78 mmHg on echographic examination (Web table1). Scheduled cesarean section was finally performed at 38 weeks gestation under low dose combined spinal-epidural anesthesia (using 2.5 mg isobaric bupivacaine + 2.5 mcg sufentanil intrathecally, followed by 37 ml of 2% lidocaine with epinephrine 1/600,000 epidurally given over

45 minutes). Standard monitoring plus central venous catheter and invasive blood pressure were used. She remained stable in the postoperative period and was discharged from the intensive care unit 2 days later.

Case #7 (year 2000):

She was 29 years old, gravida 1. She had a congenital heart disease-associated PAH stabilized after surgical repair of an interventricular septal defect when she was 3 years old. Subsequently, she had no long-term treatment because her mPAP returned to near normal value (28 mmHg). Her pregnancy was uneventful and she had a spontaneous vaginal delivery with breach presentation at 36 weeks gestation under low dose epidural analgesia. She worsened in the postpartum period and was then stabilized with the implementation of epoprostenol infusion therapy.

Case #8 (year 2002):

She was 29 years old, gravida 2 after a therapeutic abortion for maternal deterioration at 10 weeks gestation 2 years before. She had had a congenital heart disease-associated PAH operated on when she was 6 years old (large interventricular defect repaired because of an associated growth restriction) and had a pace-maker implanted 15 years later because of an atrioventricular block. She was in NYHA functional class II - III and her mPAP was 70 mmHg before this second pregnancy. She had sodium beraprost sodium, aspirin and lisinopril as long-term treatment. At 27 weeks gestation, she had a hemoptysis and her dyspnea increased (NYHA functional class III). She was hospitalized and she remained subsequently stable under the same treatment except for aspirin, which was discontinued because of the hemoptysis. A scheduled

cesarean section was performed at 34 weeks gestation under low dose combined spinal-epidural anesthesia (using 1.25 mg isobaric bupivacaine + 2.5 mcg sufentanil intrathecally, followed by 26 ml of 2% lidocaine with epinephrine 1/600,000 given epidurally). Standard monitoring plus central venous catheter with invasive blood pressure were used and nitric oxide was introduced during surgery at 50 ppm. Nitric oxide weaning was successful on the fourth postpartum day and she remained stable thereafter with beraprost sodium and lisinopril as long-term treatment.

Case #10 (year 2002):

She was 22 years, gravida 1. She had a congenital heart disease-associated PAH and was in NYHA functional class II with a mPAP of 79 mmHg. She also had an autoimmune thrombocytopenia. She remained stable during pregnancy with 75.10^9 platelets.L⁻¹ on average. Pregnancy was well tolerated until a sudden stillbirth occurred at 36 weeks gestation during hospitalization for intravenous immune globulin treatment. After transfusion of red pack blood cells and platelets, cesarean delivery was performed uneventfully one day later under combined spinal-epidural anesthesia (using 2.5 mg isobaric bupivacaine + 2.5 mcg sufentanil intrathecally, followed by 22 ml of 2% lidocaine with epinephrine 1/600,000 given epidurally). The initial postpartum period in intensive care unit was uneventful, but her condition deteriorated on Day 6 with increasing signs of right-sided heart failure. She died the day after.

Case #11 (year 1999):

She was 28 years old, gravida 2. She had a fenfluramine associated PAH revealed by circulatory collapse at 23 weeks gestation during this second pregnancy. She was admitted in intensive care unit where norepinephrine, dobutamine and oxygen therapy were implemented. Swan-Ganz monitoring showed a low cardiac index for gestational age ($1.9 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$) and a PAP of 50/28/34 for systolic, diastolic and mean values, respectively. Nitric oxide therapy was ineffective and she died 3 days later with refractory right-sided heart failure, before therapeutic abortion could be performed.

Case #12 (year 2000):

She was 31 years old, gravida 2. She had a mixed connective tissue-associated PAH revealed during pregnancy at 20 weeks gestation by a NYHA functional class IV and a mPAP value of 46 mmHg. Nitric oxide plus dobutamine therapy was started and monitored continuously during the peripartum period with a Swan-Ganz catheter. Nitric oxide therapy was effective and resulted in a 22% decrease in mPAP. Therapeutic abortion was decided the same day and oral mifepristone was given for cervical ripening. Labor was induced with vaginal misoprostol and oxytocin infusion one day later under low dose epidural analgesia (bupivacaine 0.06% and sufentanil 0.5 mcg/ml). This was well tolerated hemodynamically. Vaginal delivery was uneventful and nitric oxide plus dobutamine weaning was easily obtained. Her condition continued to improve in the intensive care unit during the postpartum period. One week after delivery, although she was still in NYHA functional class IV, mPAP had decreased to 38 mmHg and cardiac index had markedly increased ($4.5 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$). Corticosteroid, cyclophosphamide and

oral anticoagulant were implemented and the patient was alive and still stable at the one-year postnatal visit.

Case #13 (year 2002):

She was 38 years old, gravida 5 after four early abortions. She had a human immunodeficiency virus-associated PAH diagnosed in 1995. She was in NYHA functional class II before pregnancy and mPAP was 50 mmHg. She remained stable throughout pregnancy. Cesarean section was scheduled at 34 weeks gestation and was performed (after zidovudine infusion) under low dose combined spinal-epidural anesthesia (using 2.5 mg hyperbaric bupivacaine + 2.5 mcg sufentanil intrathecally, followed by 18 ml epidural of 2% lidocaine with epinephrine 1/600,000 given epidurally). Norepinephrine ($5\text{mg}\cdot\text{h}^{-1}$ initially) was introduced during surgery because of a 750-mL intraoperative bleeding. One liter of hydroxyethylstarch was rapidly infused to compensate for the bleeding and norepinephrine could be discontinued at the same time. She remained stable postoperatively in NYHA functional class II and mPAP decrease to 35 mmHg (Web table1). Long-term anti-human immunodeficiency virus treatment was implemented thereafter with lamivudine and zidovudine.

Case #14 (year 1998):

She was 41 years old, gravida 3. She had had a previous early termination of pregnancy at 10 weeks gestation in 1996 and one earlier spontaneous abortion. Her chronic thromboembolic pulmonary hypertension was discovered in 1995 after multiple thromboembolic events associated with a heterozygous factor V Leiden mutation. She was in NYHA functional class I, mPAP was 40mmHg and she was treated with warfarin.

During pregnancy her condition deteriorated moderately, as demonstrated by a shift to NYHA functional class II and an increase in mPAP to 63 mmHg. Cesarean section was thus decided at 33 weeks gestation and performed under general anesthesia because of an associated placenta praevia. Four red pack blood cells were transfused intraoperatively to compensate simultaneously for a 1.5-L bleeding; no vasopressors were needed. The patient had a new moderate thromboembolic event diagnosed one week postpartum, which was treated by increasing anticoagulation regimen. Eleven months later, she had a thrombendarterectomy, which resulted in a full normalization of PAP (Web table1).

Case #15 (year 1996):

She was 29 years old. She had a chronic thromboembolic pulmonary hypertension after multiple thromboembolic events associated with a protein S deficiency. She was in NYHA functional class II – III and was treated with warfarin; mPAP was 26 mmHg. Her condition deteriorated during pregnancy, because of new a thromboembolic event despite prophylaxis with low molecular weight heparin. Cesarean section was performed at 33 weeks gestation under general anesthesia, because of mild on-going anticoagulation. There was no abnormal bleeding but refractory right-sided heart failure developed postoperatively and the patient died 3 weeks after delivery.