Use of Extracorporeal Respiratory Support During Pregnancy: A Case Report and Literature Review

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We describe the case of a 25 year-old woman at 27 weeks of gestation who was admitted to our intensive care unit (ICU) for acute respiratory distress syndrome (ARDS) caused by pandemic 2009 H1N1 influenza A. She presented with septic shock and refractory hypoxemia unresponsive to rescue therapies such as recruitment maneuvers, prone positioning, and nitric oxide inhalation. Extracorporeal membrane oxygenation (ECMO) for respiratory support was instituted, and the patient's clinical conditions progressively improved: she was extubated after 16 days and discharged from the ICU 3 days later. No fetal complications were observed. At 38 weeks of gestation she gave birth to a healthy baby. *ASAIO Journal* 2012; 58:281–284.

Treatment of acute respiratory distress syndrome (ARDS) in pregnant women is particularly challenging because of the high risk of death for both the mother and the fetus. In cases of refractory impairment of gas exchanges unresponsive to conventional measures, extracorporeal membrane oxygenation (ECMO) can be a life-saving maneuver, but it is a very demanding and complex technique. The clinical management of these cases is extremely challenging and has to be made in conjunction with the obstetric, neonatal, and critical care teams.

Case Description

Two days after returning from a trip to Morocco, a 25 year-old primigravida at 27 weeks of gestation presented to the emergency department with fever and dyspnea. History and physical examination were unremarkable (in particular, the body mass index was within normal limits, and there was no history of asthma, diabetes, immunosuppression, or cardiac diseases), and her prenatal course was normal. She was febrile and hypotensive (blood pressure [BP] 85/40), oxygen saturation was 86% while breathing 100% oxygen, and a chest x-ray showed a left lung infiltrate. She was admitted to the intensive care unit (ICU) with a presumptive diagnosis of community-acquired pneumonia, and therapy with ceftriaxone (Fidia Farmaceutici, Abano Terme, Italy) and azythromycin (Pfizer Italia, Latina, Italy) was started. Blood gas analysis at arrival (with an inspired oxygen fraction of 100%) showed severe hypoxemia and mixed acidosis (pH 7.24, pO_2 59.2, pCO_2 48, base excess −7, HCO_3 19.8, lactate 1.2). A chest x-ray showed extensive, bilateral infiltrates (**Figure 1**). She was intubated and ventilated with a tidal volume (TV) of 6 ml/kg ideal body weight, a respiratory rate (RR) of 40, and a positive end-expiratory pressure (PEEP) of 20 cm H_2O; plateau pressure (Pplat) was 37 cm H_2O, and respiratory system compliance (Cpl, rs) was 17 ml/cm H_2O. Recruitment maneuvers (pressure-controlled inflations of 40 and 45 cm H_2O sustained for 20 sec) and nitric oxide inhalation (up to 20 ppm) failed to obtain any improvement in gas exchanges. Despite the state of pregnancy, prone positioning was attempted without significant benefit on arterial oxygenation. Obstetric ultrasonography showed a normal fetal growth and biophysical profile; notably, no adverse effects on fetus vitality were observed during the prone positioning trial.

Bacterial cultures of blood, urine, and tracheal aspirate were negative, although a nasal swab was positive for pandemic 2009 H1N1 infection (assessed with reverse transcription polymerase chain reaction [rt-PCR]). Treatment with high-dose oseltamivir (Roche, Milano, Italy) (300 mg/day by nasogastric tube) was started; a complete course of dexamethasone (Hospira Italia, Napoli, Italy) was administered to promote fetal lung development.

One day after admission the patient remained severely hypoxemic, and a chest x-ray showed signs of barotrauma (subcutaneous emphysema and basal left pneumothorax): for these reasons, we decided to initiate an extracorporeal respiratory support by means of a venovenous bypass.

A 25 F drainage cannula was placed in the right femoral vein, and a 19 F return cannula was placed into the right internal jugular vein. Vessels were cannulated percutaneously as previously described.[1] Blood was drained from the inferior vena cava and propelled by a centrifugal pump (Jostra Rotaflow, Maquet Cardiopulmonary AG, Hechingen, Germany) through an artificial lung (PLS Quadrox, Maquet Cardiopulmonary AG). Extracorporeal blood flow was set to 3.5 L/min and sweep gas flow to 4 L/min of oxygen: the gradual correction of hypercapnia and acidosis (pCO_2 from 52.9 to 41 and pH from 7.29 to 7.39 over a period of 30 min) allowed a marked reduction of TV (from 350 to 250 ml), RR (from 40 to 10/min), and Pplat (from 37 to 30 cm H_2O), whereas a high PEEP (20 cm H_2O) was maintained to avoid excessive reduction of mean airway pressure (Paw) and consequent lung collapse or pulmonary flooding; despite the maintenance of relatively high Paw, the reduction of

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Disclosure: The authors have no conflicts of interest to report.

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DOI: 10.1097/MAT.0b013e318249695d

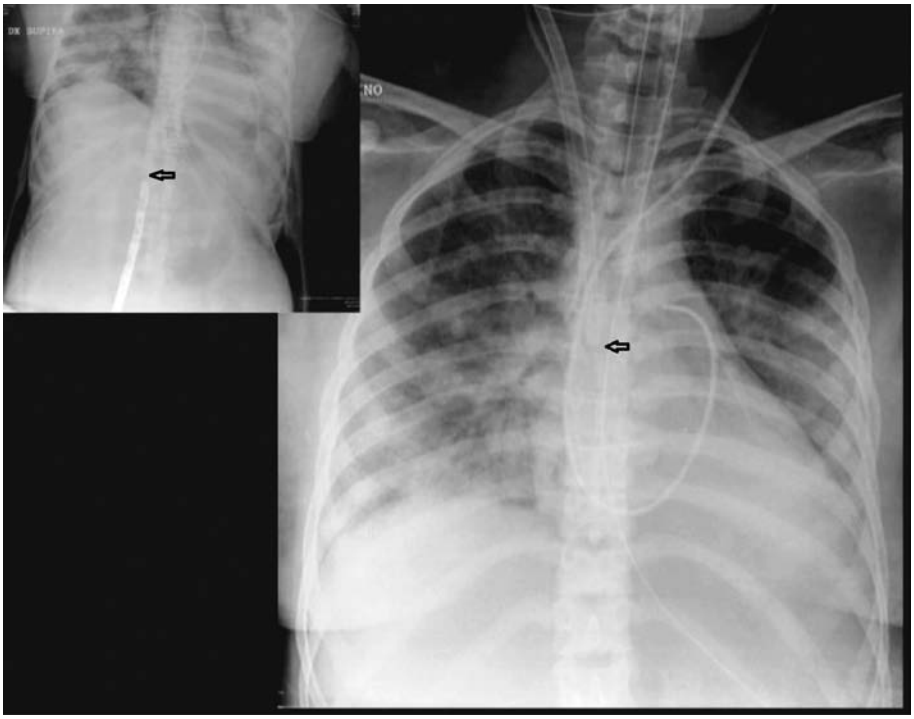

Figure 1. Chest x-ray at admission, showing diffuse, patchy infiltrates in both lungs. Arrows indicate the position of extracorporeal cannulas (in the upper left corner of the tip of the femoral cannula).

inspiratory pressures and minute ventilation avoided worsening of air leak, and no chest drainage was required.

Anticoagulation was maintained with infusion of unfractionated heparin titrated to an activated clotting time of 180–220 sec; no thrombotic or hemorrhagic complications were observed.

Cardiotocography was performed three times a day to assess fetal well-being and showed periods of low variability of fetal heart rate: sonography for biophysical profile and umbilical and middle cerebral artery Doppler evaluation remained normal, indicating that the reduced variability of fetal heart rate was a consequence of pharmacologic sedation. After ECMO institution the patient's clinical conditions gradually improved (**Figure 2**), and the extracorporeal support was withheld after 13 days. The patient was then rapidly weaned from the ventilator and extubated 16 days after admission. Pregnancy proceeded regularly until 38.2 weeks of gestation, when the patient delivered vaginally a healthy baby.

Discussion

In March 2009, an outbreak of respiratory illness caused by a novel, swine-origin influenza A H1N1 virus was identified in Mexico[2]; thereafter, the disease spread all over the world and as of April 2010 at least 17,853 deaths were reported to the World Health Organization (WHO).

Pregnancy has been recognized as an important risk factor for respiratory complications of pandemic H1N1 influenza, together with obesity, asthma, diabetes, and immunosuppression.[3]

The clinical presentation of pandemic H1N1 influenza during pregnancy is similar to that observed in the general population. In most cases the disease presents as a mild illness, but some patients develop refractory hypoxemia, frequently associated with shock and multiple organ failure.[3] Hypoxemia usually requires invasive mechanical ventilation with high PEEP and is unresponsive to rescue therapies such as prone positioning and nitric oxide inhalation.[4] In the most severe patients ECMO has been used as salvage therapy, with the aim of maintaining acceptable gas exchanges while limiting the risk of ventilator-induced lung injury.[5,6]

Experience with ECMO in pregnancy is limited. Before the influenza pandemic, ECMO had been described only in a few obstetric patients with ARDS from different causes. In a review of these cases, Cunningham *et al*.[7] observed that maternal and fetal outcomes were better in patients ventilated for less than 7 days before ECMO institution, similar to what was observed in the general adult population.

The information about the use of ECMO in pregnant patients with 2009 H1N1 influenza is scarce. In the ANZIC group experience,[8] 9 of the 64 (14%) critically ill pregnant women received ECMO, and 6 of them (67%) survived. Very recently, authors from the same Australian group analyzed retrospectively the clinical course of 12 pregnant or postpartum women treated with ECMO in seven tertiary centers. They reported a high rate of hemorrhagic complications that caused the death of three women, whereas ECMO circuit-related complications were rare; 66% of these patients survived, and the infants' survival rate was 71%.[9] In addition, some successful single cases have been reported.[10–12]

The main technical problem expected with ECMO in pregnancy is difficult blood drainage because of caval compression by the gravid uterus: emergency delivery or placement of additional venous cannulas may be required.[13] In our patient a femorojugular bypass was used, blood was drained through a femoral cannula of very large caliber (25 F), and the patient was kept in left lateral decubitus: this allowed the maintenance

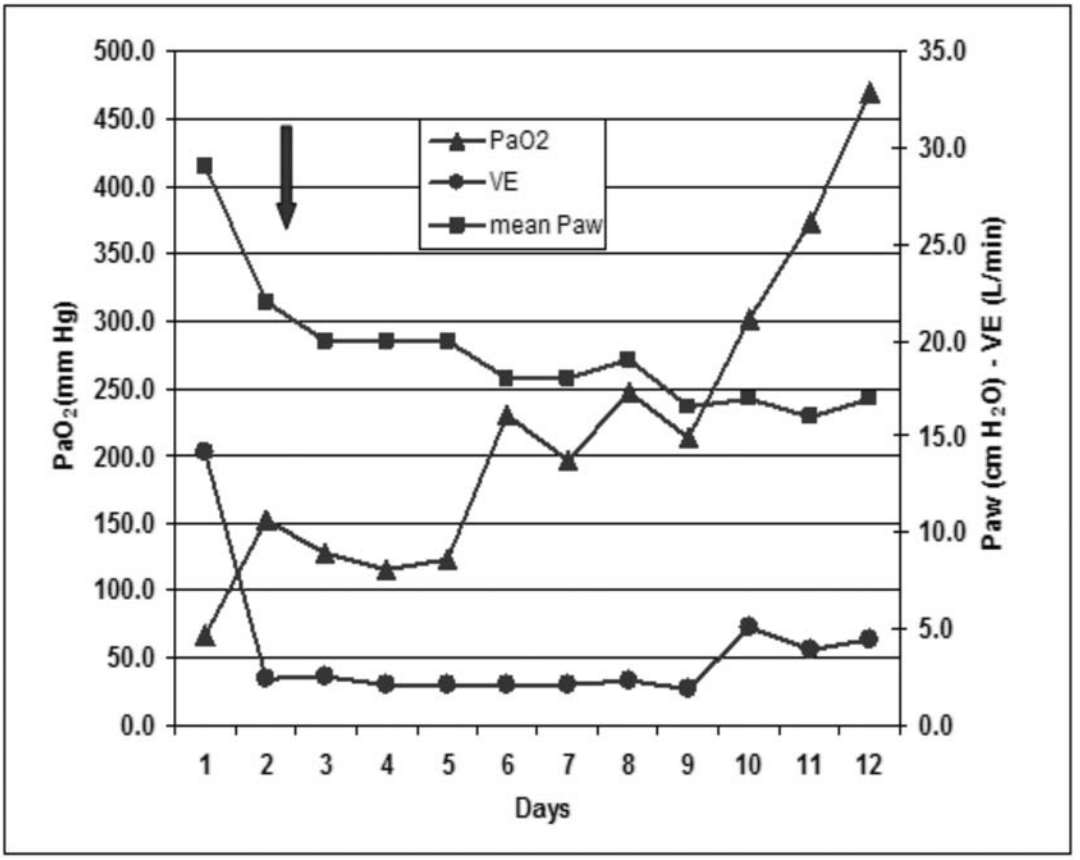

Figure 2. Variation of mean airway pressure, arterial pO_2 (PaO_2) and minute ventilation during the intensive care unit (ICU) stay. Note the important reduction of minute ventilation and mean airway pressure after the start of extracorporeal membrane oxygenation (ECMO) (arrow). Paw, mean airway pressure (cm H2O); VE, minute ventilation (L/min).

of a high extracorporeal blood flow without excessive negative suction pressures.

Patients on ECMO need to be systemically anticoagulated. Heparin has no effect on the fetus because it does not cross the placental barrier, whereas the risk of obstetric hemorrhagic complications is obviously increased.

The efficacy and safety of corticosteroids in patients with serious respiratory complications from H1N1 influenza is unclear.[14] A recent study showed an improved outcome of a very small number of patients with ARDS from pandemic H1N1 influenza receiving moderate doses of methylprednisolone.[15] Despite this, current WHO guidelines do not recommend adjuvant steroid administration (World Health Organization. Clinical management of human infection with new influenza A (H1N1) virus: initial guidance [http://www.emro.who.int/csr/h1n1/pdf/clinical_management_21_5_2009.pdf]).

This issue is particularly interesting during pregnancy, when in situations of threatened preterm labor or emergency delivery a course of bethametasone or dexamethasone is administered to promote fetal maturity. Current evidence does not suggest a negative impact of this practice on the maternal immune system.[16,17]

When caring for a critically ill pregnant woman, the most challenging issue is the selection of the appropriate timing for delivery. Delivery is expected to improve maternal condition by reducing the metabolic and cardiovascular demand associated with pregnancy. In patients on ECMO, the delivery may have the additional benefit of facilitating blood drainage. In a review of 28 pregnant women with ARDS, Catanzarite *et al*.[13] suggested that delivery is indicated during the third trimester of pregnancy or in case of deteriorating maternal conditions. Other authors caution against routine delivery, emphasizing that the risks associated with labor or cesarean delivery may be unacceptably high.[18,19] In our patient, emergency delivery was considered immediately after admission, but no clear signs of fetal distress were evident while the risk of a surgical procedure in such a critical patient was extremely high. For these reasons we found it more reasonable to postpone the delivery, considering ECMO support the best option to warrant the highest chance of survival to both the mother and the fetus. Thus, it is clear that this kind of decision is extremely challenging and has to be made on a case-by-case basis, in conjunction with the obstetric, neonatal, and critical care teams.

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