CASE REPORT

A PREGNANT WOMAN WITH AVIAN INFLUENZA A (H7N9) VIRUS PNEUMONIA AND ARDS MANAGED WITH EXTRACORPOREAL MEMBRANE OXYGENATION

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Abstract. We report a case of H7N9 avian influenza pneumonia in a pregnant woman who developed acute respiratory distress syndrome (ARDS) managed with extracorporeal membrane oxygenation (ECMO). A 29-year-old, 27 week pregnant woman developed rapidly progressive pneumonia with bilateral infiltrates on chest x-ray and was confirmed to have influenza A (H7N9) infection. Her condition deteriorated and she developed ARDS which was managed with veno-venous extracorporeal membrane oxygenation (V-V ECMO) and treated with antimicrobials. Her clinical symptoms and oxygenation gradually improved and the ECMO was discontinued on the 19th day. Unfortunately, she suddenly died a few days later, due to a presumed pulmonary embolism. Based on our experience, ECMO may be useful to manage pneumonia due to H7N9 avian influenza and ARDS in pregnant women.

Keywords: influenza A virus, H7N9 subtype, respiratory distress syndrome, adult, ECMO, pregnancy, myocarditis, pulmonary embolism

INTRODUCTION

China reported the first case of human H7N9 avian influenza A in March 2013 (Ding *et al*, 2014). Unlike infections with other H7 virus subtypes (*eg*, H7N2, H7N3, and H7N7), which usually cause mild-to-moderate disease in humans, infection with this H7N9 subtype can cause severe pneumonia and acute respiratory distress syndrome (ARDS). Pregnant women are particularly susceptible to severe complications from influenza, and have a greater mortality risk (Qi *et al*, 2014).

Conventional management of ARDS caused by H7N9 influenza infection includes an antiviral and ventilatory support. ECMO may be used to preserve life when conventional therapy fails. Several studies have found ECMO is beneficial

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in the management of ARDS in influenza patients (Cianchi *et al*, 2011; Liu *et al*, 2014) and among pregnant women with respiratory failure due to H1N1 influenza (Dubar *et al*, 2010). However, no published studies have reported the use of ECMO for managing pregnant women with H7N9 influenza and ARDS.

We describe here a 27-week pregnant woman with H7N9 influenza and ARDS treated with ECMO and discuss the use of ECMO for this indication.

CASE REPORT

A 29-year-old, 27-week pregnant woman was transferred to our hospital with acute respiratory failure on February 16, 2014. She had a history of close contact with ducks several days before symptom onset. She began having a fever of 39°C on February 10, 2014 with a heavy cough. Two days later, she became progressively dyspneic and required mechanical ventilation initiated the day before transfer to our hospital.

On admission to our hospital, her blood pressure was 125/72mmHg, her pulse was regular at 112 beats/min, her respiratory rate was 33 breaths/min, and her temperature was 36.5°C. She had an oral intratracheal tube in place. Lung examination revealed dyspnea but showed no obvious moist rales or rhonchi. Abdomen examination revealed a pregnancy with a uterine fundal height of 24 cm.

Laboratory examination showed a peripheral leukocyte count of 6,900/l with 94% neutrophils, a platelet count of 8,100/l, and a hemoglobin concentration of 9.5 g/dl. Her aspartate aminotransferase (AST) level was 105.4 μ/l (normal range <35 μ/l), but the other liver function tests were normal. Her creatine kinase isoenzyme (CK-MB) was slightly elevated at 40.5 μ/l (normal range <24 μ/l), her creatine kinase, Troponin T and brain natriuretic peptide (BNP) levels were normal; her serum creatinine level was also normal. A RT-PCR revealed H7N9 influenza infection. Her chest radiograph had bilateral pulmonary infiltrates (Fig 1). She was treated with oseltamivir 75 mg bid, meropenem 1.0 g Q8 hours, and teicoplanin 400 mg daily. Doppler ultrasound for fetal tones was normal initially and checked daily.

She was continued on a ventilator with synchronized intermittent mandatory ventilation (SIMV) with a respiratory rate of 20 times/min; a positive end-expiratory pressure (PEEP) of 10 cmH_2O; a tidal volume (Vt) of 400 ml and a fraction of inspired oxygen (FiO_2) of 100%. By day 2 of hospitalization at our hospital her PaO_2 decreased to 35 mmHg and so we decided to emergently begin ECMO using the veno-venous mode. ECMO was conducted at a bloodflow rate of 2.5 l/min and a gasflow of 4 l/min of 100% oxygen. Using the ECMO, we decreased the ventilator settings to a frequency of 10 times/min; a Vt of 300 ml; a PEEP of 10 cmH_2O and a FiO_2 of 49%. After initiation of ECMO, her PaO_2 increased to 62mmHg.

On the third day of hospitalization at our institution, the patient developed atrial fibrillation and had a large amount sputum from the endotracheal tube. The chest radiograph showed bilateral pulmonary infiltrates which had progressed from previously. Her CK increased to 509.7 μ/l (normal range <195 μ/l), her TNT increased to 332 ng/ml (normal range <100 ng/l), and her BNP increased to 22,512 ng/l (normal range <900 ng/l), suggesting myocarditis and cardiogenic pulmonary edema. The heart failure she was treated with Lasix and lanatoside C, and her atrial fibrillation was treated

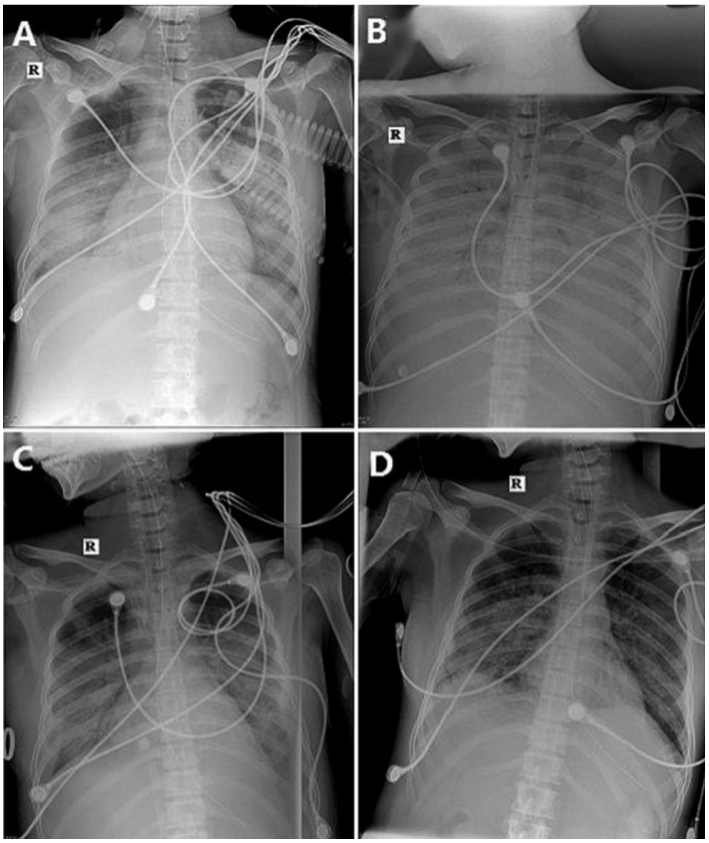

Fig 1–Chest radiograph of reported patient: A) On the 2nd day of admission; B) on the 5th day of admission; C) on the 10th day of admission; D) on the 20th day of admission.

with amiodarone. At this time no fetal heart tones was found and the fetus was thought to have died, but because of her high risk state no surgery was performed to remove the dead fetus.

On the fourth day of hospitalization, her heart failure remained uncontrolled. Her heart rate was 125 beats/min, and her BNP had increased to 35,000 ng/l. Her ECMO was changed to veno-arterial mode.

By the fifth day of hospitalization, her BNP had decreased to 15,359 ng/l and the x-ray showed a reduction in the infiltrates.

On the seventh day of hospitalization, the fetus delivered spontaneously and her vital signs remained the same. There was minimal vaginal bleeding and this stopped a few days later.

The highest temperature was 38°C during the first 2 weeks of hospitalization, but on the seventh day of hospitalization, her temperature increased to 39.5°C. Cultures of the urine, sputum and blood all grew out multidrug resistant *Acinetobacter baumannii*. The bloodflow of ECMO was reduced to 0.5 l/min and the gasflow was reduced to 2.5 l/min of 40% oxygen. An x-ray at that time showed a significant reduction in the pulmonary infiltrates.

The ECMO was discontinued on the 19th day of hospitalization and the indwelling catheter was removed. Ventilatory support was continued in the SIMV mode with a respiratory rate of 20 times/min; a Vt of 300 ml; a PEEP of 6 cmH2O and a FiO2 of 59%.

Three days later the patient's oxygenation suddenly decreased, followed by cardiac arrest. Her jugular vein was distended and an echocardiogram showed right ventricle dilation, suggesting a massive pulmonary embolism. The patient did not survive the cardiac arrest.

DISCUSSION

A successful maternal outcome after ECMO treatment for severe respiratory failure in pregnancy has been previously

reported (Dubar *et al*, 2010). However, the use of ECMO to manage ARDS in a pregnant woman with H7N9 infection has not been reported. This is the first published report for this application we were able to find in the literature. The patient improved by 18 days of ECMO but died from cardiac arrest due to a presumed pulmonary embolism.

We believe ECMO has value in the management of ARDS caused by H7N9 infection in a pregnant woman. ECMO provides adequate oxygenation when ventilator support is inadequate. H7N9 infection can cause myocarditis, and veno-arterial ECMO (V-A ECMO) can give both cardiac and respiratory support.

The complications of ECMO are usually related to bleeding rather than thromboembolism because of anticoagulation given during ECMO treatment (Buck, 2005). However, maternal coagulation is more complex, possibly increasing the risk for thrombosis. The pulmonary embolism in our case was unexpected because the patient had received systemic anticoagulation with unfractioned heparin. There are reports of thrombus formation after thrombolytic or anticoagulant therapy (Doepp *et al*, 2005; Leontiadis *et al*, 2010). Riccabona *et al* (1997) reported the overall incidence of venous clots among 30 patients treated with ECMO was 20% as measured by serial color Doppler sonography.

In our patient, the pulmonary embolism may has been caused by pulmonary artery thrombosis or embolism from a deep vein thrombosis (DVT). The morbidity of DVT is high among pregnant women (James, 2009). Thrombosis of the pulmonary artery is also possible. Sepsis may induce hypercoagulability (Jagneaux *et al*, 2004), resulting in enhanced thrombin generation, activation and fibrin formation. Pregnancy may also induce hypercoagulability (Battinelli *et al*, 2013).

Monitoring heparin therapy is important during ECMO. The activated clotting time (ACT) is commonly measured at bedside (Muntean, 1999). Some debate exists regarding the optimal range and the accuracy of point-of-care measuring devices (Bembea *et al*, 2013). We usually measure the ACT every two hours, with a goal of 160-180 seconds. The ACT may not accurately reflect the coagulation state during ECMO (Bembea *et al*, 2013). Thrombelastography (TEG) is considered to be better than prothrombin time (PT), activated partial thromboplastin time (APTT), and ACT in detecting clinically relevant clotting abnormalities in some conditions (Martini *et al*, 2008). A more reliable method may need to be used during ECMO, such as TEG.

Atypical clinical manifestations, such as heart failure, can occur in H7N9-infected patients (Wiwanitkit, 2013). In addition to the respiratory problem, this patient also had heart failure and suspected myocarditis. In our patient, pre-hospital hypoxia was present and myocardial damage due to hypoxemia may have occured. However, her cardiac condition gradually improved with treatment.

In summary, ECMO may be used in a pregnant woman with ARDS due to H7N9 infection and inadequate oxygenation along with treatment using antiviral therapy and ventilatory support. Pulmonary embolism may be a complication in addition to heart failure due to myocarditis.

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