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## Long term extracorporeal membrane oxygenation therapy for H1N1 influenza related acute respiratory distress syndrome and several complications

### H1N1 influenza ilişkili akut respiratuar distres sendromunda uzun dönem ekstrakorporeal membran oksijenatör tedavisi ve birçok komplikasyon

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#### Abstract

Extracorporeal membrane oxygenation (ECMO) has significantly advanced in recent years. During the 2009 H1N1 influenza pandemic, the use of venovenous (VV) ECMO represented a successful rescue treatment for acute respiratory distress syndrome (ARDS) in patients failing conventional ventilation techniques. The patient was thirty nine year-old and 38 weeks pregnant who had a seizure and then aspiration pneumonia occurred. Due to respiratory failure and hemodynamic instability she was intubated and vasopressor agent was initiated. Her chest X ray showed bilateral nonhomogeneous opacity; hence she was diagnosed with severe ARDS and septic shock. VVECMO was applied by a cardiovascular surgery team and the patient was transferred with the ECMO from hospital to our institution. During her hospitalization, multiple complications occurred, such as pneumothorax, critical illness polyneuropathy, clinical illness myopathy, oxygenator clotting and she was treated successfully.

**Keywords:** Acute respiratory distress syndrome, Respiratory failure, Intensive care unit, Extracorporeal membrane oxygenator

#### Öz

Ekstrakorporeal membran oksijenatörü (ECMO) son yıllarda oldukça gelişmiştir. 2009'daki H1N1 influenza pandemisi sırasında konvansiyonel ventilasyon tekniklerinin başarısız olduğu akut respiratuar distres sendromlu (ARDS) hastalarda venovenöz (VV) ECMO'nun başarılı bir tedavi olduğu gösterildi. Yirmi dokuz yaşında, 38 hafta gebe hastada sezaryen ile doğum sonrası aspirasyon pnömonisi gelişti. Solunum yetmezliği ve hemodinamik instabilite nedeniyle entübe edildi ve vazopresör ajan başlandı. Akciğer grafisinde bilateral nonhomojenöz opasite artışı gözlemlendi; bu sebeple ARDS ve septik şok tanısı aldı. VVECMO kardiyovasküler cerrahi ekibi tarafından kuruldu ve hasta ECMO ile hastanemize transfer edildi. Hastanede yatışı süresince pnömotoraks, kritik hastalık polinöropatisi, kritik hastalık myopatisi, oksijenatörün pıhtılaşması gibi birçok komplikasyon ortaya çıktı ve hasta başarı ile tedavi edildi.

**Anahtar kelimeler:** Akut respiratuar distres sendromu, Solunum yetmezliği, Yoğun bakım ünitesi, Ekstrakorporeal membran oksijenatörü

#### Introduction

In 2009, human infection with the novel influenza A/H1N1 virus was first introduced [1]. Novel influenza usually affects patients with comorbidities such as, asthma, chronic bronchitis, malignancy, transplants, obese, elderly patient and especially pregnant women [2]. H1N1 influenza also can cause severe ARDS. In 2009, during H1N1 influenza pandemic, ECMO was used for the rescue and support therapy on patients with ARDS or severe hypoxemia. 1972, an adult patient with post-traumatic respiratory failure, long-term ECMO as support for severe respiratory failure was first successfully used [3]. The usage of ECMO was abstained until the conventional ventilator support vs ECMO for severe adult respiratory failure (CESAR) trial [4]. After the CESAR trial many centers have started and continued to use ECMO.

This case report presentation is about H1N1 influenza related ARDS, and the patient was treated successfully in spite of multiple complications by using several treatment modalities.

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## Case presentation

Thirty nine year-old and 38 weeks pregnant patient was admitted to a hospital due to upper respiratory tract infection symptoms. In her postpartum period, she had a seizure attack and then aspiration pneumonia occurred and owing to respiratory failure and hemodynamic instability; she was intubated with an orotracheal intubation tube and connected to invasive mechanical ventilation (MV) and vasopressor agent was initiated. On her chest X ray showed bilateral multiple nonhomogenous opacity, the ratio of arterial partial pressure oxygen to fractional of inspired oxygen ( $\text{PaO}_2/\text{FiO}_2$ ) lower than 100% hence she was diagnosed with severe ARDS, septic shock and aspiration pneumonia (Figure 1).

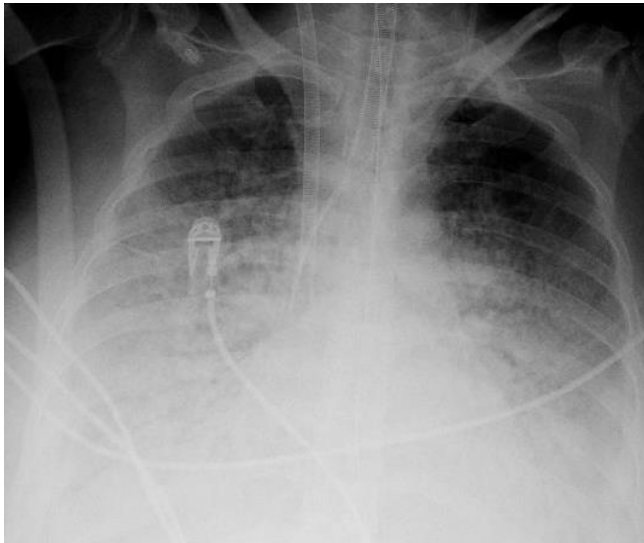


Figure 1: Bilateral nonhomogenous opacity

Broad spectrum antibiotics and antiviral therapy were initiated. Tracheal aspiration culture, blood culture, urine sample culture, a viral and bacterial panel were taken. After three days, her medical situation was getting worse and in spite of lung protective ventilation strategy arterial blood gas analysis (ABGA) showed hypoxemia,  $\text{PaO}_2/\text{FiO}_2$  ratio 40%, therefore she was referred to our hospital. When the patient was evaluated we decided to install a VVECMO. First, VVECMO was applied by a cardiovascular surgery team and then the patient was transferred with the VVECMO from hospital to our institution. Initial ECMO parameters were blood flow (BF) 4.5 L/min, sweep gas flow 3-5 L/min,  $\text{ECMOFiO}_2$  ( $\text{FmO}_2$ ) 100%. At the same time, MV mode was synchronized intermittent mechanical ventilation-pressure control (SIMV-P). MV parameters were tidal volume 6 ml/kg, respiratory rate 8-10 breath/minute, positive end expiratory pressure (PEEP) 10  $\text{cmH}_2\text{O}$ ,  $\text{FiO}_2$  30-60%, plateau pressure 20-25  $\text{cmH}_2\text{O}$ . We applied sedative, neuromuscular blocking drugs (NMBDs) and unfractionated heparin infusion during the period of ECMO. Activated clotting time (ACT) level was measure and unfractionated heparin dose was regulated as to target ACT level which was 160-220 sn. The viral bacterial panel detected H1N1 influenza virus and oseltamivir was maintained. On the twentieth day, hypoxemia deepened, ABGA had pH: 7.23,  $\text{pCO}_2$ :55.2 mmHg,  $\text{pO}_2$ : 69.5 mmHg,  $\text{HCO}_3$ : 20.3mmol/L,  $\text{SO}_2$ : 91%, according to ABGA, ECMO parameters rearranged. Consequently the membrane of ECMO was checked by ABGA and according to results, oxygenator clotting was thought and the

membrane of the ECMO was changed. During fourteen days 2mg/kg/day methylprednisolone was applied. On the twenty second, she was lain in prone position over the course of 12 hours. After the position and changing the ECMO membrane, her ABGA and chest X ray was getting better. ABGA was pH: 7.53,  $\text{pCO}_2$ :34.6 mmHg,  $\text{pO}_2$ : 82.7 mmHg,  $\text{HCO}_3$ : 28.7 mmol/L,  $\text{SO}_2$ : 97% ( $\text{FiO}_2$ :70%). After twenty five days, in spite of lung protective MV strategies pneumothorax occurred in her left hemithorax and a chest tube was placed. Five days later, pneumothorax regressed and the chest tube was removed. After thirty one days, the ECMO BF 1L/min, sweep gas flow was 1 L/min, too and MV support was maintained. ECMO was weaned on the thirty first day. Percutaneous tracheostomy was applied cause of prolonged duration of MV support and no complication occurs. After that, the sedation was discontinued. On neurologic examination she was conscious, could orient herself, and was cooperative. On the other side, bilaterally, her upper and lower extremities had loss of strength, deep tendon reflexes were not determined and she had paralysis of all her extremities. Critical illness polyneuropathy (CIP) and critical illness myopathy (CIM) were diagnosed and she was treated with physiotherapy. After the physiotherapy rehabilitation, she could move autonomously. In addition, MV support was decreased and MV mode was changed to continue positive airway pressure mode and positive end expiratory pressure 10 $\text{cmH}_2\text{O}$ , pressure support 8  $\text{cmH}_2\text{O}$ ,  $\text{FiO}_2$ :40%. After the changing mode, T tube was connected (3-4 L/min oxygen) and her chest X ray was regressed (Figure 2).



Figure 2: Bilateral opacity in regression

When  $\text{PaO}_2/\text{FiO}_2$  ratio was 350%, tracheotomy was decided to decannulate on sixty third days on stay of ICU. After the decannulation neither dyspnea nor hypoxemia occurred, hence the patient was transferred to the general ward and then was discharged from hospital to home. She was healthy in follow-up.

## Discussion

ARDS is characterized by hypoxemia and bilateral radiographic opacities, associated with increased venous admixture, increased physiological dead space, and decreased lung compliance. The mortality range of ARDS is very high. According to Berlin Definition, mortality rate was more than 50% in the severe ARDS group patients [5]. There are countless

reasons to become ARDS. One of them is H1N1 influenza virus that plays a role in the etiology of ARDS. In this presented case, severe ARDS occurred due to H1N1 influenza infection in her postpartum term. In this case our first aim recovered hypoxemia, ensured the oxygen delivery to tissues and to buy time until her clinical situation was getting better. ELSO guidelines suggest that during VVECMO for ARDS the achievement of  $\text{SaO}_2 > 80\%$  and  $\text{SvO}_2 > 70\%$  indicates adequate support [6,7]. In the presented case, although lung protective strategies and hemodynamically support had been supplied, ABGA showed severe hypoxemia  $\text{PaO}_2/\text{FiO}_2$  ratio  $< 100\%$  hence we decided to implement VVECMO. During acute respiratory failure VVECMO can be used as a rescue therapy to buy time until improvement of the underlying disease. VVECMO is used to supply oxygenation and  $\text{CO}_2$  removal, or both while the lungs recover, or as a bridge to transplant in case of end stage lung disease [8]. During H1N1 pandemic of 2009 and 2010 the German ARDS Network reported their research. 116 patients were identified who had H1N1 disease and 61 of them received ECMO. The overall mortality was 38%; among patients receiving ECMO, the mortality was 54% [9]. The patient was accepted with VVECMO installed in another hospital and she was transported by ECMO team. The patient's safety is dependent on the adherence to transport's team and protocols. Our ECMO team consisted of two cardiovascular surgeons, two anesthetists, a nurse and a perfusionist. In the literature a retrospective case series is about mobile ECMO team has consisted of two intensivists, an ICU nurse and a perfusionist, too [10]. Prone position is another treatment modality well-known procedure to increase oxygenation in patients with ARDS under MV. Guervilly et al. [11] informed during VVECMO therapy, fifteen patients with ARDS turned to prone positioning and didn't occur any major complications. In this presented case, prone positioning was performed three times during 12 hours while VVECMO was being applied. We detected that ABGA and radiological imagination were better than supine positioning. Undergoing with VVECMO, the movement can become very difficult and health risk for the patients. When the patient moves unstrained, the cannula can remove or kink. The bleeding complication or oxygenator clotting or blocking ECMO system can occur. Hence sedative or NMBDs can be administered which have several beneficial influences on ARDS patients with ECMO. Especially in the early period of VVECMO, sedation helps during the secure transfer of the patient. On the other hand NMBDs, immobilization and malnutrition can cause muscle weakness, atrophy CIP and CIM. In our case NMBDs were administered during VVECMO. After ECMO removed, we detected NMBDs related to CIP and CIM. There are many factors for CIP/CIM such as hypotension, hypoxia, hyperpyrexia, aminoglycosides, renal failure, renal replacement therapy, duration of ICU stay, vasopressor and inotropes support, NMBDs and corticosteroids [12]. In the literature a pediatric patient with ARDS who has CIP and CIM to perform active rehabilitation while on VVECMO and successfully recover [13]. In this case she possessed lots of risk factors. As distinct from our patient couldn't perform active or passive rehabilitation during VVECMO that's cause of NMBDs administration. For the treatment to CIP and CIM, drugs therapy was stopped at first and then the passive physical therapy

and then active physical therapy were performed. After the rehabilitation she could move by herself.

In the literature, there are many of case reports which have H1N1 influenza virus related ARDS and ECMO was used. The most important difference between these cases and this case is one of the prolonged stay with VVECMO cases and the other important situation is administration of patient with ECMO to ICU. Movement with ECMO is very hard and has a health risk. During the ECMO period, anticoagulant therapy was administered so tracheostomy was not applied earlier and the prolonged intubation and MV duration were the other problems. Another impressive point is a lot of complications which were CIP and CIM, pneumothorax but despite all of this difficultness, she was treated successfully.

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