

Extracorporeal Membrane Oxygenation Experience in the Patient with Acute Respiratory Distress Syndrome After *Candida pneumonia*

Candida Pnömonisi Sonrası Akut Solunum Sıkıntısı Sendromu Hastasında Ekstrakorporyal Membran Oksijenasyonu Deneyimi

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Abstract

Acute Respiratory Distress syndrome (ARDS) is an acute, diffuse, inflammatory lung injury that leads to increased pulmonary vascular permeability, increased lung weight and loss of ventilated tissue. Since the definition of ARDS, more than 40% of the mortalities is caused by it despite the significant developments in the management of severe ARDS. The patients who used extracorporeal membrane oxygenation (ECMO) for severe ARDS treatment had lower morbidity and mortality rates. In this case report, a patient with coronary artery disease in whom severe ARDS and septicemia were developed after *Candida pneumonia* and was treated with ECMO was presented.

Öz

Akut Solunum Sıkıntısı sendromu (ARDS) pulmoner vasküler geçirgenlikte artış, akciğer ağırlığının artması ve havalanan doku kaybına yol açan akut, yaygın, enflamatuvar bir akciğer hasarıdır. Ağır ARDS, ilk tanımlanmasından bu yana yönetimindeki önemli gelişmelere rağmen, %40'tan fazla mortaliteye neden olmaya devam etmektedir. Ağır ARDS tedavisinde ekstrakorporeal membran oksijenasyonu (ECMO) yapılan hastalar daha düşük morbidite ve mortalite oranlarına sahiptir. Bu olguda koroner arter hastalığı olan *Candida* pnömonisi sonrası ARDS ve sepsisemi gelişen hastada ECMO tedavisi uygulanmıştır.

Introduction

Acute Respiratory Distress Syndrome (ARDS) is an acute, diffuse, inflammatory lung injury that leads to increased pulmonary vascular permeability, increased lung weight, and loss of ventilated tissue. ARDS diagnostic criteria include new or worsening respiratory symptoms within a week, bilateral opacities that are compatible with pulmonary edema and cannot be explained by other reasons in chest X-ray or computerized tomography (CT) in the lack of heart failure or loading of excessive fluid to explain respiratory failure and the rate of arterial oxygen pressure (PaO_2)/fraction of inspired oxygen (FiO_2) ≤ 300 when positive end-expiratory pressure (PEEP) is ≥ 5 cmH_2O . When PEEP is ≥ 5 cmH_2O with mechanical ventilation, if $\text{PaO}_2/\text{FiO}_2$ is ≤ 100 , it is defined as severe ARDS (1). Despite the significant developments in the management of severe ARDS since its definition, it causes more than 40% of the mortalities (2).

Extracorporeal membrane oxygenation (ECMO), which is a kind of extracorporeal life support (ECLS), provides oxygenation and carbondioxide elimination in one of two main configurations, either venoarterial (VA) or venovenous (VV). VV ECMO is used mostly in adult patients and represents 78% of ECLS use in this population (3). The patients who used ECMO for severe ARDS treatment had lower morbidity and mortality rates (1). In this case report, a patient with coronary artery disease in whom ARDS and septicemia were developed after *Candida pneumonia* and who was treated with ECMO was presented. However, the patient died on the 7th day of her admission to the intensive care unit.

Case Report

A 78-year-old woman with diabetes mellitus, hypertension, coronary heart disease, coronary stent and thyroidectomy was admitted to the intensive care unit. Her general condition was poor, she was confused, Glasgow Coma Scale (GCS) score was 11 and the oxygen saturation was low (SpO_2 : 80-90). Informed consent was obtained from the patient and relatives. There were bilateral diffuse ground-glass infiltrations in the chest X-ray. The auscultation of the lungs revealed bilateral coarse crackles.

The arterial blood gas (ABG) showed pH: 7.2, pO_2 : 35 mmHg, pCO_2 : 67 mmHg and SaO_2 : 57, she

was intubated and followed-up with synchronous intermittent mandatory ventilation in pressure support mode on FiO_2 : 100% PEEP: 15 cmH_2O in mechanical ventilator.

A 12 F central venous catheter was placed and the patient was anaesthetized with 0.4 mg/kg/hour propofol infusion. In the following hours, the mode was switched to pressure-regulated volume control and recruitment maneuver was applied to the patient. Noradrenaline infusion of 0.15 mcg/kg/min was added to the treatment of the hypotensive patient and in addition to piperacillin + tazobactam treatment, levofloxacin was added.

According to the trans-thoracic echocardiography, pulmonary arterial pressure was 60 mmHg. The patient who was considered to have right heart failure and pulmonary hypertension was started on clopidogrel and sildenafil treatment. The culture from the bronchoalveolar lavage taken with bronchoscopy reported *Candida* growth. Anidulafungin was started to the patient with multiorgan failure such as hepatic and renal failure.

We decided to start VA ECMO support when the ABG of the patient showed pH: 7.15, pO_2 : 50.9 mmHg, pCO_2 : 72 mmHg, SaO_2 : 82. ECMO catheters were placed to the left femoral artery and vein. After the heparine bolus of 80 u/kg, the maintenance infusion was started at the dose of 18 u/kg/hr. The efficacy of the administered heparine was controlled with activated clotting time (ACT). The ACT was tried to be kept between 150-200. In the follow up, anisocoria was detected in the patient. The GCS was 3-4 so cranial CT was obtained. In cranial CT, a probably acute hemorrhage area with focally characterized diffuse areas of parenchymal hemorrhage which reached to 7.5 cm at the widest diameter, which was hypodense centrally with a peripheral hyperdense rim that was considered to belong to the hemorrhage and which was at the level of corpus callosum in the middle line and extending partially to the opposite hemisphere, which occurred on the basis of a possible infection or old hemorrhage was observed in left frontal region. There was acute hematoma in the left at the level of basal ganglia and diffuse hemorrhage in the ventricles. There was diffuse hemorrhage also within the cerebellar folia, bilateral sylvian fissures with the right side being more prominent and in the

subarachnoid spaces in the bilateral fronto-parietal regions.

Discussion

ARDS was firstly defined in 1967. Ashbaugh et al. (4) reported a mortality rate of 58% in 12 patients with ARDS. Gille and Bagniewski (5) collected data from 7 countries, 233 ARDS patients were treated with ECMO by 90 health care providers. The cumulative survival rate was 15%.

Between 1986-2006, Brogan et al. (6) examined the registry of Extracorporeal Life Support Organization, which is an international network, to create the first major international multicenter database of ECMO for severe ARDS. That registry included 1.473 patients with a mean age of 34 years and their 78% were treated with VV-ECMO for the mean duration of 154 hours. The discharge rate and overall survival rate were 50%. Mortality associated risk factors were advanced age, decrease in the patient's weight, prolonged ventilation time before ECMO, arterial blood pH being lower than 7.18, underlying reason of respiratory failure and the complications of ECMO. VV ECMO was associated with increased survival compared to VA ECMO. About 9% of patients had radiographic findings related to cerebral infarction, bleeding or brain death (6).

The most important complication of ECMO in the first years was bleeding. Knoch et al. (7) showed surface-heparinized ECMO circuits and membranes reduced daily blood loss and required intravenous heparin dose. The survival rate was higher in patients treated with heparinized systems. During ECMO treatment, in a study using standard anticoagulation therapy with unfractionated heparin as continuous infusion followed by repeated measurements of ACT or activated partial thromboplastin time (APTT), ACT values were found to be within the range of 180-220 second and the target APTT level was desired to be at least 1.5 times higher than the upper limit of the normal reference interval (8). Heparin and albumin coated cannulas were used in our patient. Heparin dose was regulated with ACT follow-ups and it was kept between 150-200.

Intracerebral hemorrhage or infarction in ECMO is a devastating and often fatal complication that occurs 10% to 15% of patients with ARDS (9). In the the Australian and New Zealand-ECMO series, 43% of deaths were associated with intracranial hemorrhage

(ICH) (10). Seventy-four adults who received VA ECMO at a single center, the ICH rate was 18.9%. ICH risk increases with female gender, heparin use, renal insufficiency, dialysis need and most importantly, in correlation with thrombocytopenia. Mortality was 92.3% in patients with ICH whereas 61% in non-ICH patients (11). The emergence of ICH in the patient who fulfilled all criteria increased the risk of mortality.

The most important complication may be infection and sepsis. The large surface of the synthetic material is prone to colonization and infection. Of ECMO patients, 79% died from multi-organ failure or septic shock (12). The risk of bacteremia and fungemia is high in ECMO patients, because blood is in contact with artificial surfaces on which bacteria and fungi can easily spread. Cannulas allow skin bacteria to enter the bloodstream. There are no guidelines regarding prophylactic antibiotic or antifungal therapy for ECMO (13). Coagulase-negative *Staphylococci* and *Candida* species are common causes of ECMO-associated bloodstream infection, and the risk of infection with *Stenotrophomonas maltophilia* and *Aspergillus* species may increase in patients with long-term ECMO treatment (14). Despite the initiation of the treatment for *Candida pneumonia* in our case, perhaps the ECMO treatment has increased the risk of septicemia.

The incidence of right ventricular failure (RVF) in ARDS was reported as 9.6%-25%. The main reason for the development of RVF in ARDS is the increased pulmonary vascular resistance (PVR). Mechanical ventilation with PEEP also causes increase of PVR (15). In the studies on hemodynamic variables of pulmonary hypertension related RVF and survival with pulmonary arterial hypertension, low cardiac index and high mean right atrial pressure were observed to be associated with poor survival (16). When RV failure develops, VV ECMO can be changed to VAV mode to evacuate RV volume and RV shear stress, or VAV mode is preferred for the treatment of RVF and ARDS (17). VA ECMO mode was preferred in our patient with pulmonary hypertension and RVF.

Severe ARDS is associated with high morbidity and mortality rates in patients treated with mechanical ventilation in intensive care units. In recent years, the marked advances in ECMO technology have led to safer initiation and maintenance of this life-saving

treatment and reduced its risks regarding the patients. However, further well-designed, randomized clinical trials are needed before widespread use of treatment is accepted in suitable patients with severe ARDS.

Ethics

Informed Consent: Informed consent was obtained from the patient and relatives.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.S.Ö., A.C., M.O., Design: E.S.Ö., A.C., M.O., Supervision: M.O., Fundings: E.S.Ö., A.C., M.O., Materials: E.S.Ö., A.C., Data Collection or Processing: E.S.Ö., A.C., Analysis or Interpretation: E.S.Ö., A.C., M.O., Literature Search: E.S.Ö., A.C., M.O., Critical Review: M.O., Writing: E.S.Ö., A.C.

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