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CASE REPORT

# Successful use of venovenous extracorporeal membranous oxygenation in a 22-month old boy with necrotizing pneumonia, osteomyelitis and septic shock caused by Panton Valentine leukocidin – producing Staphylococcus aureus

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## ABSTRACT

*Extracorporeal membrane oxygenation (ECMO) is a life saving treatment for patients with severe respiratory failure. We present a case of a young child with invasive Panton Valentine leukocidin-producing Staphylococcus aureus infection, which is responsible for severe and invasive infection with a high mortality rate, commonly associated with necrotizing pneumonia. Our patient presented with septic shock and necrotizing pneumonia leading to severe respiratory failure, refractory to conventional ventilation means. After 1-day of treatment, venovenous ECMO (VV ECMO) was successfully instituted and inotropic support was gradually decreased. Acute renal failure was managed with peritoneal dialysis and intermittent venovenous hemofiltration. The patient was weaned from ECMO 9-days later and was mechanically ventilated for another 3 weeks. Necrotizing pneumonia with pleuropulmonary complications was finally managed by videothoracoscopy with evacuation of debris and partial pleural decortication. Osteomyelitis was confirmed by positron emission tomography – computed tomography (PET-CT) and was surgically treated. The child was treated with antistaphylococcal antibiotic therapy for 54 days. Finally, he was discharged to a rehabilitation center without supplemental oxygen and with his neurologic status at his baseline. Our case shows that VV ECMO can be applied to children with severe bacterial pneumonia resistant to conventional ventilation strategies and with moderate circulatory failure.*

**Key words: extracorporeal membranous oxygenation, septic shock, Staphylococcus aureus pneumonia, Staphylococcus aureus, Panton Valentine leukocidin, child**

## Introduction

Extracorporeal membrane oxygenation (ECMO) is a life saving treatment for patients with severe respiratory failure, when conventional means of support are inadequate. Furthermore, ECMO also protects lungs from ventilator-induced lung injury, commonly associated with aggressive mechanical ventilation. (1) Venovenous ECMO (VV ECMO) has several advantages over venoarterious ECMO (VA ECMO) and should be used in the management of severe respiratory failure in children, when possible. VV ECMO could be applied even in respiratory failure associated with mild to moderate myocardial dysfunction, since cardiac output can be improved with adequate oxygenation and lower intrathoracic pressures. (1,2) Hypox-

emic and hypercapnic respiratory failure can be both successfully managed with VV ECMO. The most common causes for VV ECMO support in children, beside neonates, are viral and bacterial pneumonia, acute respiratory distress syndrome (ARDS), asthma and aspiration of blood, gastric acid and foreign substances. (1)

Recently, the incidence of severe infections caused by Staphylococcus aureus has been increasing. This increase has been postulated to be due to the emergence of strains encoding new virulence factors, among which Panton Valentine leukocidin (PVL) toxin has been most commonly studied. (3) PVL is produced by 2% of S. aureus isolates and causes white blood cell (WBC) lysis and tissue necrosis. (4)

## Case report

A 22-month-old boy, with an uneventful medical history and up to date immunization, was admitted to the Department of Infectious Diseases, at the University Medical Centre Ljubljana, because of a two-day history of high grade fever (up to 39 °C) and painful swelling of the right hip. Ultrasound examination revealed effusion in the right hip joint, but only a minute amount of serohaemorrhagic fluid was evacuated from the joint and sent for culturing. Antibiotic treatment with cefotaxime and flucloxacillin was started. Despite supplementation with oxygen, he developed respiratory failure and septic shock (respiratory rate 80/min, oxygen saturation 85–90%, blood pressure 70/45 mmHg, heart rate 190–200/ min, capillary refill time 4–5 seconds) and hence was transferred to the tertiary pediatric intensive care unit (PICU) (Department of Pediatric Surgery and Intensive Care, University Medical Centre Ljubljana).

Immediately after admission (day 0) he was intubated and mechanically ventilated with pressure-controlled ventilation. Treatment of septic shock was continued initially with fluid resuscitation (crystalloids). Inotropic support with dopamine and vasopressor support with norepinephrine was started soon after. Norepinephrine was changed to epinephrine after 4 hours with addition of sodium nitroprusside for the cold shock and hydrocortisone was added for 7 days. Blood products (red blood cells, platelets and fresh frozen plasma) were administered when needed according to guidelines. (5) Initial laboratory evaluation revealed: WBC 0.8 x$10^9$/L, CRP 269 mg/L, PCT 209 $\mu$g/L and hemoglobin 104 g/L, lactate 2.2 mmol/L. Initial arterial blood gas analysis on mechanical ventilation was: pH 7.15, $pCO_2$ 47 mm Hg, $pO_2$ 75 mmHg (fraction of inspired oxgen, $FiO_2$ = 1.0), base excess = -12.4 mmol/L, bicarbonate 15.9 mmol/L. Respiratory failure was severe, and despite high pressure ventilation (peak inspiratory pressure (PIP) 42 cm $H_2O$ and positive-end expiratory pressure (PEEP) 12 cm $H_2O$) a $FiO_2$ 1.0 was needed. High-frequency oscillatory ventilation (HFOV) was started and inhaled nitric oxide 20 ppm was added, without improvement. Respiratory failure was worsening with hypoxemia (arterial $pO_2$ 56 mmHg; mean airway pressure (MAP) 28; Oxygenation index (OI) 49.6) and severe hypercapnia ($pCO_2$ 107 mmHg) (figure 1). After 24 hours of modulation of respiratory treatment we started VV ECMO (QUADROX PLS oxygenator, ROTAFLOW centrifugal pump; Maquet) (day 1), using 14-Fr venous canellas in the right internal jugular vein and right common femoral vein. PVL-positive methicillin-sensitive S. aureus was grown from blood cultures and joint fluid, but not from tracheal aspirates. Since the isolate was PVL-positive, the antibiotic treatment was changed from flucloxacillin to clindamycin and rimfapicin in order to minimize toxin production. Acute renal failure with oliguria accompanying shock (max creatinine 152 $\mu$mol/L, max urea 45.8 mmol/L) was managed with peritoneal dialysis and intermittent venovenous hemofiltration. The hemofiltration system was added sequentially to the ECMO system. We first tried to wean the ECMO on day 8, but because of right sided pneumothorax, which was successfully drained, it was prolonged to day 9. After ECMO weaning and decannulation, the patient remained mechanically ventilated on different modes of mechanical ventilation for approximately 3 weeks.

Bilateral alveolar infiltrates were seen on initial and following chest radiographs and chest computed tomo-

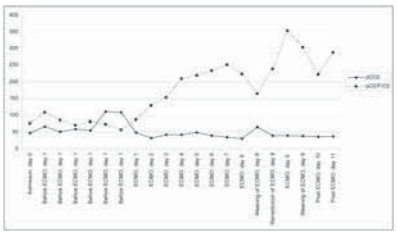

**Figure 1. Partial pressure of arterial carbon dioxide (paCO2) and ratio of partial pressure of arterial oxygen and fraction of inspired oxygen (paO2/FiO2) curves in the patient before, during and after treatment of severe respiratory failure with veno-venous extracorporeal membranous oxygenation.**

graphic scan on day 16 showed bilateral necrotizing pneumonia with abscesses and pneumatocoele formation, and persisting pleural effusion with a small pneumothorax on the right side despite a chest drain (figure 2). Streptokinase was applied intrapleurally through the right sided chest drain three-times, resulting in improved drainage of the fluid. However, control chest computed tomographic scan on day 24 showed no improvement of lung pathology. Finally, videothoracoscopy with evacuation of debris from the right plural space and partial pleural decortication was performed on day 41. Pseudomonas aeruginosa was isolated from the evacuated debris and the patient was treated with ceftazidime for 10 days. After the procedure, his clinical condition improved significantly.

Because of clinical signs of osteomyelitis of the right femur, the boy had frequent radiological, ultrasound and magnetic resonance (day 12) imagings, but with no discernible signs of osteomyelitis. After respiratory and hemodynamic stabilization, positron

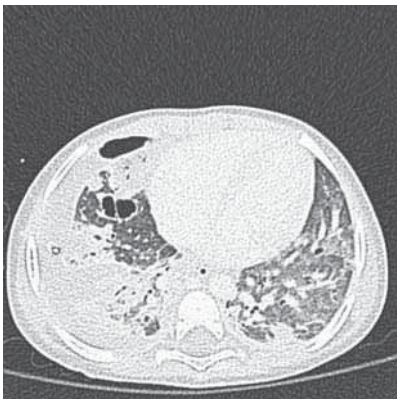

**Figure 2. Chest computed tomography scan showing bilateral lung disease with abscesses and pneumatocoeles and pleural effusion with pneumothorax on the right side; necrotizing pneumonia.**

emission tomography – computed tomography (PET-CT) was done on day 25, which eventually revealed osteomyelitis of the right femur. On day 26 arthrotomy of the right hip with forage of the right femur was done. Tissue swab, obtained during this procedure, was positive for S. aureus eubacterial DNA using the Polymerase chain reaction (PCR) method. We continued with antistaphylococcal antibiotics (flucloxacillin/clindamycin alternatively with linezolid and rifampicin) for 54 days altogether. Deep vein thrombosis of the right femoral vein, which was recognized on day 1, was treated with enoxaparin subcutaneously.

After 51 days of treatment in the intensive care unit, the patient was transferred to the surgical ward for another 23 days and then to a rehabilitation centre. At that point, he was receiving no supplemental oxygen, antibiotic treatment was completed and his neurologic status was at his baseline, apart from decreased passive and active mobility in the right hip and knee. The patient had partial necrosis of the fingertips of the feet and hands, which occurred during centralization of the blood flow in the first days of septic shock.

## Discussion

This is the first case of severe pneumonia in a child managed by VV ECMO in our institution, which is the only institution in Slovenia capable of providing extracorporeal life support techniques in children. (6) Our patient was infected with a PVL positive strain of S. aureus causing necrotizing pneumonia and osteomyelitis leading to respiratory and circulatory failure, accompanied by acute renal failure.

ECMO was first used for management of term newborns with respiratory failure (7). Later the indication and patient selection for this unconventional therapy evolved significantly and is constantly changing. Today ECMO is used for three main distinctive groups of patients: neonates with respiratory failure refractory to conventional management, neonates and children with circulatory failure and for children with respiratory failure. (1,2,7) Respiratory failure in children was the latest indication introduced for ECMO and use of ECMO for this group of patients has increased steadily, leveling off in the nineties, but recently it has been reported to be slightly increasing again. (2,8) The survival of pediatric respiratory ECMO is 50–55%. (8) There are no fixed inclusion criteria for pediatric respiratory ECMO, and ECMO is usually started if there is a high probability of a lethal outcome despite maximal conventional therapy. Lung disease should be considered to be reversible; the patient should be mechanically ventilated for less than 14 days; and no other organs major complications (significant neurologic morbidity, ongoing hemorrhagic condition, or multiple organ system failure) should be present when starting ECMO. (1,7,8). Unlike neonates, OI is not as predictive for ECMO use in children and is not tightly used for guiding the indications for pediatric respiratory ECMO. (7) In our patient the etiology of respiratory failure was potentially reversible; he was mechanically ventilated for only 24 hours; he had profound hypercarbia; his OI was more than 40; and his $p_aO_2/FiO_2$ ratio was less than 75 mmHg. When we decided to start ECMO, we considered that there was a high probability of death with conventional support. Therefore, the majority of proposed inclusion criteria for pediatric respiratory ECMO, which are sometimes used, (7,8) were met in our patient.

Community-acquired infections with PVL toxin producing S. aureus are rare, but often invasive and associated with toxic shock-like illness, necrotizing pneumonia with complications (pneumatocoeles, recurrent pneumothoraces, pleural effusion, empyema and lung abscesses), and osteoarticular infections with venous thrombosis (3,9-13) as in our patient. There are some reports of fatal outcomes in infections with S. aureus in children, although the presence of PVL toxin was not usually investigated. (14,15) In the seminal article by Gillet et al. the case fatality rate of patients with PVL-positive staphylococcal pneumonia was 75%. (16) Children infected by PVL-positive S. aureus usually die because of respiratory or combined respiratory and circulatory failure. (14,15) ECMO presents a possibility to change the outcome in life-threatening cases and ECMO use is increasingly reported in children infected with S. aureus. (17) Stroud et al. recently described two children infected by PVL-positive S. aureus, who were successfully supported with VA ECMO. (3) We decided for VV ECMO despite circulatory failure in our patient, since he was stabilized on the first day with inotropic support. Furthermore, there are several advantages of VV ECMO compared to VA ECMO: prepulmonary oxygenation with elevation of mixed venous saturation and diminishing the effect of intrapulmonary shunts, sparing of the carotid artery, maintaining full pulsatile blood flow, trapping of potential emboli in the pulmonary vascular bed and ability of percutaneus cannulation, although in our patient the cannulation was surgical. (1,18) Our decision to start VV ECMO proved to be correct, since after the institution of VV ECMO we could gradually lower the inotropes, although no direct cardiac support was delivered by VV ECMO. In adults

VV ECMO is usually used in cases of severe respiratory failure caused by PVL-positive S. aureus. (19)
In conclusion, VV ECMO is successful unconventional respiratory support in children with respiratory failure due to different etiologies. Our case shows that VV ECMO can be applied for children with severe bacterial pneumonia resistant to conventional ventilation strategies with moderate circulatory failure.

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