Life Saving Extracorporeal Membrane Oxygenation Support Use in Neonatal Listeriosis

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Neonatal early onset sepsis, before 3 days of age, is one of the most lethal perinatal events, complicating 0.5–1/1000 of deliveries, with higher rates in late preterm infants [1]. About 0.5% of cases are caused by *Listeria monocytogenes*, a ubiquitous facultative intracellular gram-positive bacteria. Listeriosis in the neonate may present as preterm labor, respiratory distress, severe sepsis, meningitis, or a characteristic rash known as granulomatosis infantisepticum. Mortality rates described in the literature are between 20% and 60%. In a study done in Israel, 1/7 of infected neonates died, and 3/7 were born before term and survived [2]. In recent years, extracorporal membrane oxygenation (ECMO) support has emerged as an optional treatment for critically ill patients. Neonates are the largest population treated with ECMO, consisting of treatment of approximately 40% of patients so far. Treatment is mainly due to cardiac congenital malformations, meconium aspiration syndrome, congenital diaphragmatic hernia, and persistent pulmonary hypertension. Sepsis is a less common indication for ECMO treatment in neonates. By January 2017, 2915 neonates had been treated with ECMO worldwide due to sepsis [3]. We describe a case of a newborn with severe neonatal *Listeria* sepsis who was treated with ECMO in our unit and survived.

PATIENT DESCRIPTION

The patient was a 36 1/7-week, 2550 gram female neonate, born following an uneventful pregnancy, except for maternal hepatitis B virus carrier status. Delivery was by emergent cesarean section due to maternal fever of 39.9°C, meconium stained amniotic fluid, and non-reassuring fetal monitor with tachycardia and decreased variability. Apgar scores were 6 and 9 at 1 and 5 minutes, respectively. Soon after delivery, the infant presented with respiratory failure, was intubated, and required respiratory support by high frequency ventilation and nitric oxide. In addition, epoprostenol sodium and sildenafil were administered for the treatment of pulmonary hypertension, and vasopressor support was started due to hemodynamic instability. Chest X-ray showed diffused pulmonary infiltrated bilaterally with normal cardiothymic contour. Initial blood count was normal (hemoglobin 15.5 g/dl, white blood cells 7430 cells/µl, platelets 241 K/µl), and C-reactive protein level was 50 mg/L. Antibiotic treatment with ampicillin and gentamicin was given following blood cultures.

Despite massive vasopressor treatment, including adrenaline (0.8 mcg/kg/min), dopamine (20 mcg/kg/min), dobutamine (20 mcg/kg/min), and vasopressin (0.0002 mcg/kg/min), the infant had resistant low blood pressure (mean pressures of approximately 29 mmHg), and signs of hypoperfusion: lactic acid level >150 mg/dl (normal range 6–18 mg/dl) with decreased urine output (< 1 cc/kg/hour). Cardiac echocardiogram showed normal cardiac structure, poor function, and a large ductus arteriosus with right to left shunt and systemic level pulmonary hypertension. Results of placental culture and neonatal blood culture revealed *L. monocytogenes*.

Due to severe uncompensated shock, ECMO support was initiated at 24 hours after birth. Arterial blood gas (umbilical line) prior to initiation demonstrated a pH of 7.23 (normal range 7.35–7.45), $PaCO_2$ of 37.4 mmHg (normal range 36–44 mmHg), PaO_2 of 54.5 mmHg (normal range 60–110 mmHg), oxygen saturation 93.8%, HCO_3 of 15.2 mmol/L (normal range 20–28 mmHg), and lactic acid level >150 mg/dl. Oxygenation index was 14.3 (FiO_2 75%, mean airway pressure 14 cm H_2O). The infant required ECMO support for 84 hours, including hemofiltration because of renal failure.

On the sixth day of life, she was weaned off ECMO support, with no major apparent complications. In the following days, vasopressors, respiratory support, and oxygen could be weaned. The patient was given *Listeria*-active antibiotics for 14 days. Repeated blood cultures were consistently negative.

Neurologic evaluation during hospitalization demonstrated a normal infant with mild eating and sucking difficulties that improved prior to discharge. A brain magnetic resonance imaging revealed enlarged ventricles and mild edema of the white matter, with no additional focal findings. Brain Stem Response Audiometry (BERA) was normal. The infant was discharged home at

the age of 6 weeks. Neurologic follow up at 8 months of age was normal except for mild hypotonia and gross motor developmental delay.

COMMENT

L. monocytogenes is a life threatening infection in neonates. It is considered to be a food-borne infection; thus, outbreaks are characteristic. Maternal symptoms may range from mild flu-like symptoms to full blown disease with fever and diarrhea, and may lead to placental infection and preterm labor. Neonatal infection, as described before, results in sepsis and may involve multiple organs, including the brain and lungs. We describe a case of severe neonatal listeriosis treated successfully with ECMO.

The introduction of ECMO has opened a new possibility for the treatment of severely unstable neonates. However, sepsis in not a common indication, reflecting only less than 10% of neonates treated with ECMO so far. Only 72% of ECMO-treated neonates survived. Survival rates vary between a few indications for ECMO, ranging from 33% in cardiac arrest to 91% in cases of meconium aspiration syndrome [3].

Neonatal sepsis may require treatment with ECMO due to several mechanisms, including hypoperfusion and pulmonary hypertension. In our case, both hemodynamic and respiratory instability were prominent, as the infant demonstrated hypoperfusion, sepsis, and pulmonary hypertension as a result of infection. Only scarce data are available regarding neonates who were treated with ECMO due to infection with *L. monocytogenes*.

Hirschl et al. [4] described nine neonates treated with ECMO for severe respiratory failure due *to L. monocytogenes* pneumonia. In their cohort, only one was a preterm infant, weighing less than 3 kilograms. The indication for ECMO in this study was mainly respiratory, although hemodynamic decompensation was also reported.

In addition, various parameters were different from the course of treatment we experienced. In the previous cohort, the median duration of treatment was 210 hours, the shortest being 137 hours. According to the Extracorporeal Life Support Organization, the average run time in cases of neonatal sepsis is 180 hours. However, our patient was supported for a shorter period (84 hours) and was weaned off as hemodynamic stability was established. Longer treatment exposes the patient to higher risk of complications.

Regarding the right time to start the support, in the cohort by Hirschl [4], infants were placed on ECMO at a median age of 70 hours. The group also discussed whether earlier transport and ECMO intervention might have improved the outcome. ECMO support in the described patient was initiated early, as soon as it was obvious that hemodynamic support was not effective. This finding strengthens the importance of early recognition of suspected neonatal listeriosis and consideration of transport if needed.

Hirschl et al. [4] reported a survival rate of 66%, much higher than 10–20% predicted prior to ECMO support. Kattan et al. [5]000 g and gestational age ≥ 35 wk reported about 52 neonates treated with ECMO in Chile due to refractory hypoxic respiratory failure, including a case of neonatal listeriosis, who did not survive.

While it may increase the survival of septic neonates dramatically, ECMO use has significant risks in neonates, such as metabolic disturbances (24%), massive bleeding (24%), and CNS infarction or hemorrhage (up to 14%) [3].

CONCLUSIONS

In our case, the decision to use ECMO was made as a last resort, as the child's circulatory shock was refractory to all other measures, and this case may suggest that the treatment was beneficial. Consequently, we recommend considering early ECMO support for neonates with *L. monocytogenes* associated hemodynamic decompensation. Evaluation of efficacy and long-term effects in comparable clinical scenarios is still needed.

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"I've learned from experience that the greater part of our happiness or misery depends on our dispositions and not on our circumstances"

Martha Washington (1731–1802), American first First Lady of the United States

"All opinions are not equal. Some are a very great deal more robust, sophisticated, and well supported in logic and argument than others"

Douglas Adams (1952–2001), English author, screenwriter, essayist, humorist, satirist and dramatist; author of the *Hitchhiker's Guide to the Galaxy* series