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Fulminant *Neisseria meningitidis*: Role for Extracorporeal Membrane Oxygenation

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ABSTRACT

Invasive meningococcal disease is often associated with complications of septic shock and central nervous system dysfunction. Extracorporeal membrane oxygenation is more commonly being used for respiratory failure and sepsis, but neurologic injury and potential coagulopathy are often considered relative contraindications. We report a successful case of complicated *Neisseria meningitidis* septic shock with disseminated intravascular coagulopathy requiring extracorporeal support.

INTRODUCTION

Each year an estimated 1400 to 2800 cases of meningococcal disease occur in the United States, for an incidence of 0.5 to 1.1 cases per 100,000 population and with a case fatality rate of 10% to 14%. Meningococcal disease also causes substantial morbidity: 11% to 19% of survivors have sequelae (eg, neurologic disability, limb loss, and hearing loss) [Bilukha 2005]. The clinical manifestations of meningococcal disease are variable and range from fever and bacteremia, to fulminant disease, sepsis, and death within hours of symptom onset. Recent data suggest that extracorporeal membrane oxygenation (ECMO) can be clinically beneficial for the treatment of severe respiratory failure, compared with conventional ventilator management [Peek 2009]. As experience and indications broaden, unconventional applications challenge traditional paradigms. We report a successfully treated case in which ECMO was used as rescue therapy for severe respiratory failure caused by overwhelming sepsis with *Neisseria meningitidis*.

CASE

The patient is a 29-year-old woman who was relatively healthy other than a history of asthma and who presented to an outside hospital with fever to 103°F, chills, flu-like symptoms, and a worsening shortness of breath. On admission, she had tachycardia to 140 beats/minute, hypotension (90/40 mm Hg), leukopenia with 2300/μL white blood cells and 31% bands, thrombocytopenia (platelets, 54,000/μL), a lactate concentration of 3.7 mg/dL, and pH of 7.2. The patient required mechanical ventilation, and her clinical picture rapidly deteriorated to adult respiratory distress syndrome with a nearly complete "whiteout" of her lungs (Figure 1). Initial blood cultures were positive for *Neisseria meningitidis* (serogroup C), and a lumbar puncture was deferred because of the coagulopathy. No other cultures were positive. Because of the worsening hypoxemia, acidosis, and hemodynamic instability, the patient was transferred to our institution on her second hospital day for consideration of ECMO. On the patient's arrival, values for her arterial blood gas variables on 100% oxygen, a peak end-respiratory pressure of 20 mm Hg, and an assist-control setting of 24 while she was sedated and pharmacologically paralyzed were as follows: pH, 7.32; PCO_2, 51 mm Hg; PO_2, 43 mm Hg. In light of her young age, previously normal neurologic

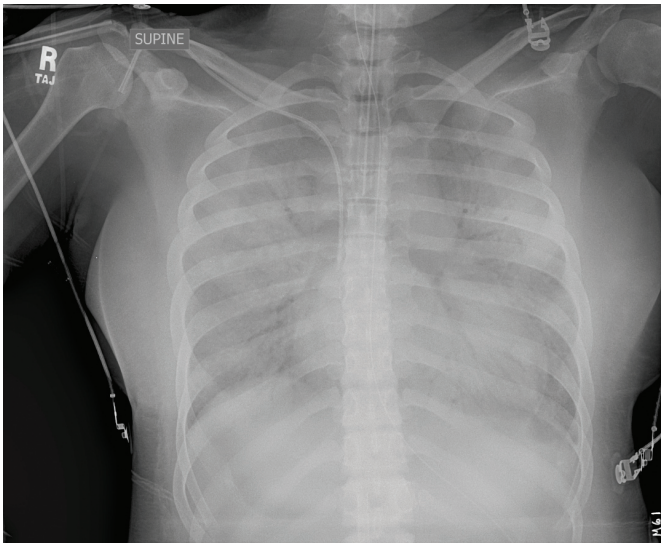

Figure 1. Chest x-ray at the time of the patient's admission to our center just prior to extracorporeal membrane oxygenation.

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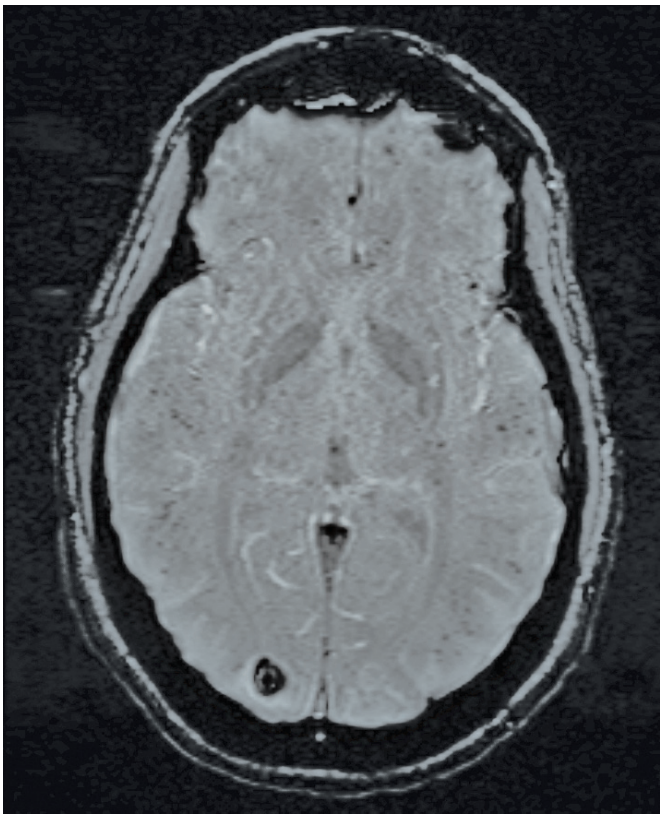

Figure 2. Magnetic resonance imaging performed on hospital day 14.

status, and worsening physiology, emergent femoral vein–femoral vein percutaneous ECMO was initiated with a BioMedicus BP-80 pump and tubing circuit (Medtronic, Minneapolis, MN, USA) and a Quadrox D oxygenator (Maquet, Wayne, NJ, USA) as follows: initial flow, 6 L/min; gas sweep, 6 L/min; oxygen concentration, 100%). She was anticoagulated intravenously with 7500 U heparin at the time of cannulation and was maintained on intravenous heparin administration at 5 U/kg per hour for the first 24 hours, with heparin administration titrated to a partial thromboplastin time of 40 to 60 seconds while the patient was on ECMO. The partial thromboplastin time ranged from 33 seconds to ≥180 seconds but was mainly therapeutic. The patient's systemic oxygenation rapidly improved, and the patient was sustained on minimal ventilator settings (fraction of inspired oxygen, 0.4; ventilator rate, 10 breaths/minute; peak end-respiratory pressure, 5 mm Hg). By ECMO day 8, the patient's chest radiograph and oxygenation had improved, thereby allowing for weaning of ECMO flows and oxygen support. Later that day, however, she sustained a grand mal seizure that responded to anticonvulsants (fosphenytoin) and benzodiazepines. The results of a computed tomography scan of the head were unremarkable. The next morning, she was successfully removed from ECMO support with minimal ventilator support. A magnetic resonance imaging analysis of the brain on hospital day 9, however, showed a small area of ischemic injury and innumerable tiny microhemorrhages (Figure 2) throughout the brain, which prompted additional concerns for possible meningitis. Despite this result, the patient was extubated within 72 hours without any evidence of neurologic deficit. Pulmonary function tests performed before discharge (hospital day 14) showed a mild impairment in diffusion (diffusing capacity of the lung for carbon monoxide, 75% of predicted) and a minimal restrictive defect (forced vital capacity, 2.29 L, 66% of predicted; forced expiratory volume in 1 second, 2.1 L, 71% of predicted; total lung capacity, 3.12 L, 66% of predicted). The patient was discharged on hospital day 14 to home with her family to complete the course of ceftriaxone and phenytoin. Six days later, the patient was seen as an outpatient. She was weak, but the results of her physical examination were normal. At the 3-month follow-up visit, the patient reported normal function and neurologic capacity and has had no additional seizures.

DISCUSSION

The use of ECMO for cardiogenic shock and/or respiratory failure is a well-established salvage therapy with acceptable short- and long-term outcomes [Smedira 2001; Peek 2009]. Nevertheless, concerns about its implementation with systemic anticoagulation have contraindicated its use in this application because of the inherent risk of bleeding-related complications [Lewandowski 2000]. Our recent experiences with ECMO for patients requiring multiple surgical debridements for necrotizing soft-tissue infections have encouraged our center to be aggressive in otherwise young, healthy patients with sepsis who are dying [Firstenberg 2010]. Fortunately, the level of anticoagulation can be minimized with current oxygenators, particularly in those who receive veno-venous support, are actively bleeding, or are at risk for bleeding. In situations in which cardiac function is normal and in patients who require minimal vasoactive or inotropic support (typically for shock or acidosis), veno-venous support is preferred, because the risks of arterial cannulation and complications of systemic anticoagulation can be additionally minimized.

Another relative contraindication to ECMO is central nervous system injury [Lewandowski 2000]. Neurologic complications are not infrequent with ECMO and are associated with a poor prognosis, but they are not uniformly fatal [Kasirajan 1999]. Although we were unaware of the presence of this patient's hemorrhagic strokes upon presentation, central nervous system involvement and coagulopathy are also common in patients with invasive *Neisseria meningitides* [Stephens 2007]. This patient's profound respiratory system failure and our concern that other salvage therapies (ie, prone or oscillator ventilation) would not have provided the immediate support required in such a rapidly deteriorating young patient prompted our use of ECMO. Furthermore, the results of her pulmonary function tests also suggested that ECMO could be successfully used without the severe barotrauma associated with high-pressure ventilator support and acute respiratory distress syndrome [Peek 2009].

CONCLUSIONS

ECMO support should be considered in cases of profound and refractory respiratory failure. This case was a desperate situation for which ECMO has historically been considered a contraindication because of the potential for central nervous system injury and coagulopathy. Our successful use of ECMO with such a positive outcome in this patient with invasive *Neisseria meningitidis* and sepsis clearly favors its use in such cases.

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