A Successful Case of Extracorporeal Membrane Oxygenation As a Bridge to Recovery

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Presentation: A 50-year-old male with no known medical history presented to clinic for one year of progressive dyspnea on exertion. His family later confirmed patient was actively using methamphetamines. He was found to be in respiratory distress and was admitted to a community hospital, where he was intubated for acute hypoxic respiratory failure. Following intubation, he became hemodynamically unstable, required 3 vasopressor infusions, and had ongoing hypoxia with an oxygenation saturation of 88% on maximum ventilator support. Labs were notable for serum drug screen positivity for amphetamines and alcohol. Transthoracic echocardiogram (TTE) was performed and showed dilatation of the right ventricle (RV), an intra-atrial shunt, and elevated estimated pulmonary arterial (PA) systolic pressures. Our tertiary care center was contacted for extracorporeal membrane oxygenation (ECMO) and transfer for management of pulmonary hypertension (PH) with right heart failure and refractory hypoxia.

Assessment: The patient was initiated on veno-venous (VV) ECMO with improvement in hypoxia, and his vasopressor requirements decreased. TTE was performed on transfer and showed massive dilatation of the RV, intracardiac shunt on bubble study, and RV systolic pressure estimated at 32 mm Hg (Figure 1). Transesophageal echocardiogram (TEE) showed a 6.5 mm patent foramen ovale (PFO) with a large right-to-left shunt seen with color Doppler (Figure 2). Patient underwent right heart catheterization (RHC) (Figure 3) showing a PA pressure of 65/30/42 mm Hg with a pulmonary capillary wedge pressure of 15 mm Hg and a pulmonary vascular resistance of 5 Wood units (difficult to interpret due to use of ECMO). No significant change was noted with inhaled nitric oxide vasodilator challenge. Computed tomography angiography (CTA) of the chest was performed and no thromboembolic disease or pulmonary parenchymal disease was identified, but an enlarged PA and RV dilatation was appreciated. The patient was unable to undergo ventilation-perfusion (V/Q) scan at this time.

Monitoring and Management: The PH team was consulted for further management and the patient was started on continuous infusions of furosemide and epoprostenol starting at 2 ng/kg/min on hospital day 3 and titrated to 8 ng/kg/min by day 5 with significant clinical improvement. On hospital day 6 the patient was decannulated. Epoprostenol was further titrated to 10 ng/kg/min, and the patient was extubated on hospital day 12. The patient was not a candidate for intravenous home medication due to active substance abuse and was therefore transitioned to combination oral therapy with sildenafil and ambrisentan. TTE was repeated once on oral therapy and showed minimal right-to-left shunting through the PFO. Hospitalization was prolonged by delirium and on hospital day 32 patient was discharged to home. He was seen 2 weeks later in clinic and was found to have World Health Organization (WHO) functional class II symptoms, with brain natriuretic peptide (BNP) down to 93. He reported medication compliance, no side effects, and had abstained from methamphetamine and alcohol use since discharge. The patient was suffering from a gout flare at that time and deferred 6-minute walk test.

Key Words— bridge to recovery, dyspnea, extracorporeal membrane oxygenation, methamphetamine, pulmonary arterial hypertension

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Figure 1: Dilated right atrium (RA) and right ventricle (RV) [left image] and positive bubble study suggesting intracardiac shunt (right image).

Figure 2: Large PFO (left image, see arrow) and shunt through PFO by color Doppler (right).

Figure 3: (A) RHC pulmonary arterial waveform. (B) RHC waveform with catheter wedged in the pulmonary artery (pulmonary capillary wedge, or PCW). In this PCW waveform, respiratory variation is present during an assisted breath during mechanical ventilation. As the patient initiates the breath and creates a negative deflection in the tracing, the arrow marks “end expiration,” where an accurate PCW measurement should be obtained.
Discussion: Our patient has methamphetamine-associated pulmonary arterial hypertension (meth-APAH). The association between methamphetamine use and pulmonary arterial hypertension (PAH) was first noted in case reports dating back to the 1990s. In 2006, Chin et al published a 340-patient retrospective cohort study showing patients with idiopathic pulmonary arterial hypertension (IPAH) were 10 times more likely to have a past exposure to methamphetamines compared to patients with chronic thromboembolic pulmonary hypertension (CTEPH). Currently the updated clinical classification of PH, published in 2013, classifies methamphetamines as a “likely” cause of drug-induced PAH, compared to higher classifications of “definite” for anorexigens and “probable” for cocaine. A 2017 90-patient prospective cohort study from Stanford University also found a strong association and characterized presentations and prognosis of meth-APAH. The mechanism of meth-APAH is not known, but is presumed due to the similarities in chemical structure between methamphetamine and anorexigens, with both having activity at serotonin receptors.

Patients with PH and RV failure have been postulated to have a survival benefit if they have a coexisting PFO. Theoretically a PFO would offload right-sided pressures and increase left ventricular preload through right-to-left intracardiac shunting. While some investigators did find that patients with PH and PFOs awaiting transplant had improved survival rates compared to those without PFOs, other retrospective studies did not find a survival difference in those patients with PFOs. Nonetheless, it is not appropriate to close a PFO in a patient with moderate to severe PH, especially with any evidence of RV failure. Though the presence or absence of a PFO has not been shown to change survival, it has been observed as a cause of significant hypoxia in patients with severe PH. In our patient a large right-to-left shunt through a PFO resulted in profound refractory hypoxia, especially in the setting of intubation. Multiple case studies support our finding that medical management in patients with refractory hypoxia due to right-to-left shunting can resolve hypoxia. Our patient was started on epoprostenol and right-sided pressures improved, causing decreased shunting and allowing him to leave the hospital breathing ambient air.

Our patient exemplifies a situation in which ECMO can be used as an effective “bridge-to-recovery” (BTR) model. ECMO has been used increasingly more in the treatment of acutely decompensated PH to bridge patients to a more definitive endpoint. Three such models are “bridge to transplant” (BTT), “bridge to delivery” (BTD), and BTR. BTT is the use of ECMO until a patient can receive a lung transplant. Though the use of ECMO for BTT had unfavorable outcomes in initial studies, a 2014 review reported more favorable results as clinicians gain more experience and competence with ECMO. ECMO is also used in a BTD model for patients with PAH who decompensate during pregnancy. In our case, ECMO was used as a BTR model. BTR is the use of ECMO in patients with decompensated right heart failure while medications are titrated or causes of decompensation are reversed. This model is synonymous with other titles used in other publications such as “bridge to improvement,” or “bridge to treatment.” Though large studies are lacking, a promising collection of case series and case reports suggests this is a feasible option in well selected patients, such as our treatment-naive patient. The most extensive review of BTR patients analyzed 16 such patients. The patients who survived were far less likely to have arrested prior to cannulation and all had either reversible causes of decompensation or were not medically optimized at the time of their decompensation. A number of the patients who survived BTR were, like our patient, treatment-naive. Other cases of BTR echo this paradigm of the importance of selecting patients with reversible causes of decompensation or those who are not medically optimized. BTR may represent a viable option for patients similar to ours.

Teaching Points:
1. PFO can be a cause of profound hypoxemia in patients with RV failure from PH.
2. Shunting from right to left can be greatly improved with combined management of PH and RV failure.
3. PFO should not be closed in a patient with severe PAH with RV failure, as it would cause rapid increase in right-sided pressures and lead to acute RV failure and hemodynamic instability.
4. Epoprostenol remains first line as rescue medication for very severe PH.
5. Transition from epoprostenol to oral combination therapy was successful in our patient, as the patient required only low doses of epoprostenol to have significant effect. Of note, this is not a recommended approach in patients with high requirements of epoprostenol, nor should this be attempted outside an intensive care setting.
6. ECMO can be used as a bridge to transplant, bridge to delivery, or bridge to recovery.
7. Selection of patient for ECMO as a bridge to recovery is most successful in patients who are either not medically optimized or in patients with a reversible cause of decompensation.

References
6. Nootens MT, Beraducci LA, Kaufmann E, Devries S, Rich S. The prevalence and signifi-

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Pennsylvania) provide the centerpiece to the issue through their updates on the PHCC program and the PHA Registry (PHAR). These intertwined projects have been in development for more than 5 years and are leading the charge for center-based care and a focus on improving the quality of care for PH patients in the United States. They discuss the genesis of these endeavors and highlight the early achievements, while also identifying ongoing challenges.

As part of the journal’s enduring commitment to the members of the Pulmonary Hypertension Professional Network (PHPN), Traci Houston and Glenna Traiger provide an excellent “roadmap” to accreditation for prospective PHCCs. With their vast experiences as center coordinators and as members of the PHCC Review Committee, they are well poised to provide sage advice about the various stages of the accreditation process, from the initial application all the way through the site visit. Finally, I had the immense pleasure of facilitating an insightful roundtable discussion centered on the evolving PH patient, the complexity of PH care, and the impact of contemporary center-based care. I’m particularly proud to have recruited a multidisciplinary panel for the roundtable, including a long-time PH patient.

I think you’ll find this to be a very unique and timely issue of *Advances in Pulmonary Hypertension*. I hope you’ll have a deeper appreciation of some of the challenges we face as a community and how a renewed dedication to center-based care and quality improvement will help us meet these challenges in the coming decades. And perhaps another disease-centered community (in 20 years) will look upon what we’re currently doing in PH as a guiding light for their own cause.

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