

Successful use of veno-venous extracorporeal membrane oxygenation for acute chest syndrome in a child with sickle cell disease and SARS-CoV-2

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Abstract

Children with sickle cell disease (SCD) are at increased risk for severe illness due to severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2). We describe the successful native lung recovery of a child with SCD referred for lung transplant (LTx) evaluation who was on prolonged veno-venous extracorporeal membrane oxygenation (VV-ECMO). He initially presented with acute chest syndrome complicated by SARS-CoV-2 infection that ultimately required dual-lumen, single bicaval VV-ECMO cannulation for respiratory support. Despite increased risk of hemolysis and thrombosis from SCD and SARS-CoV-2 infection, he was successfully supported on VV-ECMO for 71 days without complications leading to native lung recovery with meticulous management of his SCD therapy. This report provides new insight on our approach to VV-ECMO support in a child with SCD and SARS-CoV-2 infection. With a successful outcome, the patient has returned home but still on mechanical ventilation with LTx still an option if he is not eventually liberated from invasive respiratory support.

Introduction

Sickle cell disease (SCD), a hereditary recessive hemoglobinopathy, disproportionately affects the African-American population and is associated with vaso-occlusion, such as acute chest syndrome (ACS).¹ The severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) global pandemic has negatively impacted children with SCD, leading to more intensive care unit admissions and increased mortality.² In children with acute respiratory distress syndrome (ARDS) due to SARS-CoV-2, there is a quickly rising need for extracorporeal mechanical oxygenation (ECMO) support.³ Notably, ECMO in SARS-CoV-2 increases risk of thromboembolism and coagulopathy, which is heightened in children with SCD.⁴ The literature shows that ECMO use in the SCD population is increasing, but a lingering degree of uncertainty persists given their underlying propensity for hemolysis, stroke, and thrombosis.⁵ In this correspondence, we report the successful prolonged use of veno-venous ECMO (VV-ECMO) as a bridge to recovery in a child with SCD who developed refractory ARDS due to SARS-CoV-2.

Case Description

An 11-year-old, 40kg, boy with sickle cell anemia (HbSS), asthma, and obstructive sleep apnea was transferred to our End-stage Lung Failure Program for consideration for ECMO bridge to lung transplant (LTx). Upon initial presentation at the local facility, he was diagnosed with ACS due to SARS-CoV-2 and received supplemental oxygen, corticosteroids, convalescent plasma, and remdesivir, but his hypoxemia worsened despite the escalation of maximum conventional mechanical ventilation and proning. His chest X-ray showed diffuse bilateral airspace opacities and a large pneumomediastinum from the significantly high ventilator pressures (Figure 1A). To sustain life, he underwent cannulation of the right internal jugular with a 27 Fr dual-lumen, single bicaval catheter on hospital day 15 for VV-ECMO. Over the next three weeks, there was

no evidence of lung recovery with multiple failed VV-ECMO weaning trials. Therefore, he was transferred to our institution on ECMO day 43. To maximize rehabilitation, a tracheostomy was placed for liberation from sedation. While at our institution, a total of six exchange transfusions were performed to strictly target a hemoglobin S (HbS) level [?]15% to minimize the effect of sickled red blood cells (RBCs) (Figure 2). Routine transfusions were performed per our institutional ECMO protocol with packed RBCs and Fresh frozen plasma (FFP) with extended blood group matching for the E, Kell, and Duffy antigens to minimize the risk of alloimmunization. His VV-ECMO course was uncomplicated without major bleeding or thrombotic events. Surveillance echocardiograms showed stable right ventricular pressure and function. The intensive physical rehabilitation and maximal enteral nutrition via gastrostomy tube significantly improved his deconditioning and allowed for weaning of VV-ECMO support. He was successfully decannulated after 71 days of VV-ECMO. On post-decannulation chest X-ray, he had bilateral patchy airspace opacities but with marked improvement from his pre-ECMO appearance (Figure 1B). Due to his complicated course, hydroxyurea therapy was re-initiated while on ECMO and maximized with an increase of fetal hemoglobin (HbF) levels from 0.3% to 11.5% during three months of therapy. He was also transitioned to enoxaparin therapy for an additional 2 weeks upon ECMO decannulation and then to apixaban during hospitalization given an increased risk of thrombosis due to SCD and SARS-CoV-2. After completing inpatient rehabilitation, he was ultimately discharged home with chronic mechanical ventilation five months after his initial presentation.

Discussion

ACS is one of the leading causes of mortality and morbidity in patients with SCD.⁶ Given the propensity of pulmonary disease in patients with SCD, any infectious process including SARS-CoV-2 can exacerbate ACS and lead to life threatening refractory hypoxemic ARDS as seen in our case through the sequestration of sickled RBCs. With limited data detailing SARS-CoV-2 in children with SCD, our case illustrates key elements that provide a treatment strategy for ECMO support which allowed this patient to recover but also allowed for rehabilitation to improve his candidacy for LTx.

As the ECMO circuit can exacerbate sickling and hemolysis, we believe aggressive management of the HbS level maintaining a level [?]15% while on ECMO was critical in our management and contributed to the positive outcome for this patient as we believe it prevented end organ damage from vaso-occlusive events from further sickling. Pro-active and pre-planned changes of oxygenator or circuit based on fibrin deposit burden and the free plasma hemoglobin level also prevented further hemolysis leading to end organ dysfunction or disastrous circuit failure. We also maximized the hydroxyurea therapy to increase the level of anti-sickling HbF level, in an attempt to minimize overall blood transfusion requirements, thereby lowering risk of allosensitization, should he later require LTx. The hydroxyurea-induced increase in HbF level also allowed liberalization of his exchange transfusion requirement to maintain HbS levels <30% upon discharge. The patient has returned home but continues to require chronic mechanical ventilation and is only tolerating a very prolonged wean from mechanical ventilation. He participates in physical rehabilitation without need for re-hospitalization, which enhances his potential for full recovery or makes his future candidacy for LTx more favorable as pre-transplant hospitalizations is associated with increased morbidity and mortality post-LTx.⁷

Conclusion

At present, there is no consensus or published guidelines on ECMO management in the sickle cell patient population; hence, there are no recommendations for this patient population with SARS-CoV-2 infection. With no immediate end in sight for the ongoing pandemic, any new information that can shed a light on clinical management of sickle cell patients with SARS-CoV-2 infection is greatly needed. Despite having SCD and SARS-CoV-2, our patient was supported on VV-ECMO for 71 days with a favorable outcome and without thrombosis, bleeding, pulmonary hypertension, end organ dysfunction, or sepsis as a bridge to recovery through a comprehensive multidisciplinary team effort.

Conflicts of Interests

The authors declare that there are no disclosures and no conflicts of interests.

References

1. Piel FB, Steinberg MH, Rees DC. Sick Cell Disease. *N Engl J Med* 2017;377(3):305.
2. Vilela TS, Braga JAP, Loggetto SR. Hemoglobinopathy and pediatrics in the time of COVID-19. *Hematol Transfus Cell Ther* 2021;43(1):87-100.
3. Di Nardo M, Hoskote A, Thiruchelvam T, et al. Extracorporeal Membrane Oxygenation in Children with Coronavirus Disease 2019: Preliminary Report from the Collaborative European Chapter of the Extracorporeal Life Support Organization Prospective Survey. *ASAIO J* 2021;67(2):121-24.
4. Malas MB, Naazie IN, Elsayed N, et al. Thromboembolism risk of COVID-19 is high and associated with a higher risk of mortality: A systematic review and meta-analysis. *EclinicalMedicine* 2020;29:100639.
5. Kuo KW, Cornell TT, Shanley TP, et al. The use of extracorporeal membrane oxygenation in pediatric patients with sickle cell disease. *Perfusion* 2013;28(5):424-32.
6. Ruhl AP, Sadreameli SC, Allen JL, et al. Identifying Clinical and Research Priorities in Sickle Cell Lung Disease. An Official American Thoracic Society Workshop Report. *Ann Am Thorac Soc* 2019;16(9):e17-e32.
7. Rudym D, Benvenuto L, Costa J, et al. What Awaits on the Other Side: Post-Lung Transplant Morbidity and Mortality After Pre-Transplant Hospitalization. *Ann Transplant* 2020;25:e922641.

