Case Report

Successful engraftment after hematopoietic stem cell transplantation with infusion of donor stem cells through the extracorporeal membrane oxygenation circuit

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Abstract

Wiskott–Aldrich syndrome (WAS) is a rare X-linked primary immunodeficiency due to mutations in the WAS gene expressed in hematopoietic cells. Hematopoietic stem cell transplantation (HSCT) is the treatment of choice when an appropriate human leukocyte antigen-matched donor is available. The use of the extracorporeal membrane oxygenation (ECMO) circuit to infuse donor cells for HSCT has not been previously published in the literature. We describe a case of a child who had successful engraftment after HSCT with infusion of the donor stem cells through the ECMO circuit.

Keywords: Engraftment, extracorporeal membrane oxygenation, hematopoietic stem cell transplantation, Wiskott–Aldrich syndrome

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Introduction

Wiskott–Aldrich syndrome (WAS) is a rare X-linked primary immunodeficiency characterized by thrombocytopenia, eczema, and immunodeficiency due to mutations in the WAS gene expressed in hematopoietic cells. The absence of functional WAS protein (WASp) leads to a severe clinical phenotype that can result in death unless treated early in life. Hematopoietic stem cell transplantation (HSCT) is the treatment of choice for WAS.[1,2] Infusion of donor cells for HSCT through the extracorporeal membrane oxygenation (ECMO) circuit has not been previously reported in the literature. We describe a case of an immunocompromised child who had successful engraftment after HSCT with infusion of the donor stem cells through the extracorporeal circuit.

Case Report

The patient was a 15-month-old male with WAS admitted to the hospital for HSCT. Our patient was found to be thrombocytopenic after birth. Genetic studies showed a four-base-pair deletion in intron-8 (c. 777+2delGAGT) and no protein expression of WAS by flow cytometry, confirming the diagnosis of WAS. His unaffected sister was not a human leukocyte antigen (HLA) match; thus, an unrelated donor would be required. During his 1st year of life, he required only two platelets transfusions for worsening petechiae and

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intermittent hematochezia. He received intravenous immunoglobulin therapy monthly and remained on prophylactic trimethoprim-sulfamethoxazole. He had no significant history of infection before transplantation. He was admitted at 13 months of age for preconditioning therapy for his HSCT, which consisted of fludarabine, melphalan, thiotepa, and antithymocyte globulin. During his preconditioning therapy, as his bone marrow was completely ablated, he developed *Escherichia coli* sepsis and was started on antibiotics. During this illness, he developed hemodynamic instability and was admitted to the Pediatric Intensive Care Unit on hospital day (HD#) 8. He developed refractory septic shock requiring intubation, volume resuscitation, inotropic support subsequently needing support, with venoarterial ECMO on HD# 9. He was cannulated with a 14-French arterial cannula in his right carotid artery and a 14-French venous cannula in his right internal jugular vein. Echocardiogram after cannulation demonstrated severely diminished left ventricular function and left atrial hypertension requiring balloon atrial septostomy. Inotropic support was weaned off within 72 h after cannulation. He required continuous renal replacement therapy (CRRT) on HD# 10 due to fluid overload. As planned, on HD# 10, he received unrelated HLA donor stem cell transplant through the ECMO circuit. He received 68 ml of ABO-mismatched cord blood transplant (8 out of 10, A antigen, DQB1 allele) with $CD34^+$ count of 4.7×10^5/kg and total nucleated cell count of 1.12×10^8/kg of cord blood unit. The cord blood was infused on the arterial side of the circuit at the first line postoxygenator over 40 min with no complications. On HD# 13, the patient was noted to have left-sided paralysis. An emergent head computed tomography showed acute intraparenchymal hemorrhages in the right posterior temporal lobe and left occipital lobe with 4 mm right to left midline shift. He was subsequently decannulated from ECMO. A brain magnetic resonance obtained on HD# 16 showed stable right greater than left occipital lobe hematomas and watershed infarction along the right parasagittal centrum semiovale. On HD# 22 (day +12 after his HSCT) he started to show signs of engraftment. On HD# 36, he was extubated. On HD# 40 (day +30 after his HSCT), his fluorescence *in situ* hybridization XY showed 100% donor cells. He continued to require CRRT and was transitioned to peritoneal dialysis on HD# 57 and discharged to the floor on HD# 69. His neurologic examination as well as his renal function continued to improve and he was discharged home on HD# 94. His peritoneal catheter was removed 10 days after discharge. One year later, he has recovered from his neurologic injury with no sequelae and has remained asymptomatic from the WAS standpoint. He continues to have complete donor engraftment with no evidence of mixed chimerism and without signs of chronic graft versus host disease. Figure 1 represents the white blood count, absolute neutrophil count, and major events during hospital course.

Discussion

WAS is a rare X-linked primary immunodeficiency characterized by thrombocytopenia, eczema, immunodeficiency, and increased incidence of malignancies and autoimmunity. The disease is due to mutations in the WAS gene which is exclusively expressed in hematopoietic cells. Mutations in the WAS gene have various effects on the level of WASp expression, which correlates with the variability in the disease's severity. The absence of functional WASp leads to a severe phenotype that can result in death unless treated early in life. HSCT is the treatment of choice though recent advances in gene therapy have made this therapy a reasonable alternative for patients who lack an appropriate HLA-matched donor.[1,2] ECMO is a form of cardiopulmonary bypass for patients with respiratory, cardiac, or combined cardiopulmonary failure unresponsive to conventional treatment. The use of ECMO for life-threatening complications related to HSCT has been minimally reported,[3-5] and good outcomes are limited to case reports.[6-9]

Cell therapy during ECMO support has been previously reported in a case report. Antigen-specific T-cells were infused during ECMO support in a 10-year-old child with congenital amegakaryocytic thrombocytopenia who developed adenovirus-related acute respiratory distress syndrome after T-cell-depleted haploidentical HSCT.[10] Currently, there is no literature evidence or anecdotal reports of HSCT through the ECMO circuit in adults.

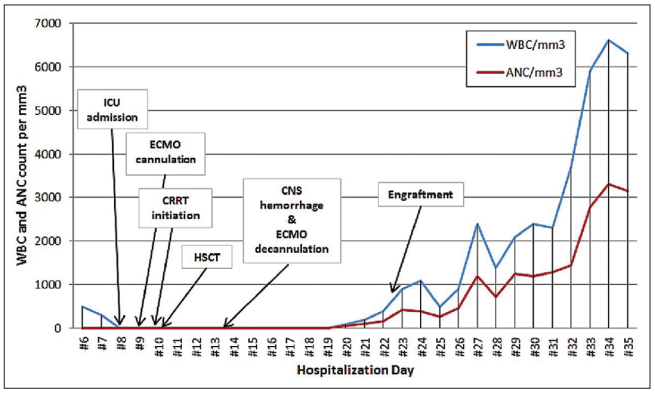

Figure 1: White blood count and absolute neutrophil count during hospital course. WBC: White blood count, ANC: Absolute neutrophil count, ICU: Intensive Care Unit, ECMO: Extracorporeal membrane oxygenation, CRRT: Continuous renal replacement therapy, HSCT: Hematopoietic stem cell transplantation, CNS: Central nervous system

However, the authors did not report the infusion site of the cell therapy. To the best of our knowledge, our case is the first report of a successful engraftment after HSCT with infusion of cell therapy through the extracorporeal circuit. The case highlights the possibility of cell therapy for HSCT when a patient is on extracorporeal support and should be feasible irrespective of the age of the patient.

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Conflicts of interest

There are no conflicts of interest.

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