ABSTRACT# 15

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Title: Successful Third Haploidentical Stem Cell Transplant After Graft Failure of Two Prior Matched Unrelated Donor Transplants in Sickle Cell Disease

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Background: Allogeneic stem cell transplantation (SCT) is the only curative option for sickle cell disease (SCD). SCT from Human Leukocyte antigen (HLA) matched sibling donors (MSD) is curative in >90% of cases but is limited by donor availability (<20%). Unrelated donors are an alternative, but fully HLA-matched unrelated donors (MUD) are rare, and unrelated donor and haploidentical transplants have increased risk of graft versus host disease (GVHD) and graft failure as compared to MSD SCT. There are reports of successful repeat SCT after graft failure in patients with SCD. However, to our knowledge, there are no reported cases of successful third SCT after two graft failures.

Methods: A 13-year-old girl with severe SCD first underwent reduced intensity MUD SCT. Fludarabine, melphalan, thiotepa, and distal alemtuzumab were used for conditioning. Tacrolimus, methotrexate, and abatacept were used for GVHD prophylaxis. Ten months later, she underwent a second MUD SCT with myeloablative conditioning, using busulfan, cyclophosphamide, and antithymocyte globulin. Tacrolimus and methotrexate were used for GVHD prophylaxis and letermovir for CMV prophylaxis. Finally, she underwent an emergency rescue haploidentical peripheral blood SCT from her mother on D+60 post second SCT. She received ATG, fludarabine, cyclophosphamide, and total body irradiation (TBI) 400 cGY for conditioning, and post-transplant cyclophosphamide, mycophenolate, and tacrolimus/sirolimus for GVHD prophylaxis.

Results: She first engrafted on day 10 after transplant (D+10) but had graft failure on D+28. She recovered her autologous bone marrow, with her innate SCD afterward. After her second transplant she engrafted on D+17, had graft failure on D+32 after sudden-onset cytokine release syndrome, and remained aplastic afterward. Notably, she had no HLA antibodies to either prior donor. After her third transplant she engrafted on D+16 and had 100% donor cells on her D+30 and D+60 evaluations.

Conclusions: Factors associated with her first graft failure include reduced intensity conditioning, viral infection, and inherent cellular immunity. Her second graft failure was likely mediated mainly by cellular-level rejection. The success of her third graft was likely due to immunosuppressive effects of TBI and the megadose peripheral blood SCT. This case shows that third SCT can be effectively performed without major acute toxicities in SCD.

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