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SUSTAINED HIV-1 REMISSION FOLLOWING HOMOZYGOUS CCR5 DELTA32 ALLOGENIC HSCT

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Background:

The "Berlin Patient" underwent 2 consecutive HSCTs with total body irradiation. It is unclear which aspects of treatment contributed to this only known case of HIV cure. We report an HIV-infected male diagnosed with Hodgkin's Lymphoma (HL) who underwent allogeneic HSCT using a homozygous CCR5Δ32 donor. Nadir CD4 was 290 cells/mm³ and baseline VL 180,000 copies/ml. ART (TDF/FTC/EFV) was started in 2012. During episodes of ART interruption viral rebound and selection of NRTI resistance was seen. HL was refractory to 1st line chemotherapy and multiple salvage regimens. An unrelated CCR5Δ32 homozygous donor was identified with one allelic mismatch at HLA-B. Conditioning was initiated with Lomustine, cyclophosphamide, Ara-C and etoposide followed by 3.6 million CD34⁺ cells/kg. In vivo T-cell depletion employed anti-CD52 and GvHD prophylaxis was cyclosporine and methotrexate. ART was continued throughout (Raltegravir, 3TC, dolutegravir). The patient developed mild gut GvHD. Full donor chimerism was maintained in blood. Six months post-HSCT complete remission was observed.

Methods:

Co-receptor tropism was predicted with Geno2Pheno based on single genome sequencing (SGS). Post-HSCT PBMC were analysed by ddPCR and qPCR. Infectious virus was repeatedly analysed by qVOA. Isolated CD4⁺ T cells were experimentally infected with X4 and R5 HIV.

Results:

SGS from pre-transplant PBMC identified multiple envelope clones all with predicted R5 tropism. ART was stopped 17 months post-HSCT and plasma HIV VL remained undetectable (<1.4 copies/ml) at 33 months. ART drugs were not detectable in plasma by LC-MS. Total HIV DNA in CD4⁺ T-cells at 33 months showed 2 positive droplets in 1 out of 8 replicates (ddPCR HIV LTR, 10⁶ cells tested) and no signal in qPCR (<0.69 HIV-gag and <0.65 HIV-LTR copies/million cells). At 16 months post transplant HIV-specific Western blot was positive while p24/p31 bands were absent. VITROS detuned and avidity analysis revealed low quantity and quality of HIV antibody titers. At three time points post-HSCT qVOA showed no reactivatable virus using a total of 24 million resting CD4⁺ T cells. Post-transplant CD4⁺ T cells did not express CCR5 and were susceptible in vitro to X4- but not R5-tropic virus.

Conclusion:

Absence of viral rebound was observed for 16 months following ART interruption at 17 months after single allogeneic CCR5-Δ32 HSCT using a no irradiation approach with only mild GvHD. To our knowledge this is the longest adult HIV remission observed since the Berlin patient.