Published in final edited form as:

J Clin Immunol. 2017 January ; 37(1): 61–66. doi:10.1007/s10875-016-0360-8.

Resolution of Epstein-Barr Virus –related Smooth Muscle Tumor in a Patient with GATA2 Deficiency Following Hematopoietic Stem Cell Transplantation

Mark Parta¹, Jennifer Cuellar-Rodriguez², Alexandra F. Freeman³, Juan Gea-Banacloche³, Steven M. Holland³, and Dennis D. Hickstein⁴

¹Clinical Research Directorate/Clinical Monitoring Research Program, Leidos Biomedical Research, Inc., NCI Campus at Frederick, Frederick, Maryland, 21702, ²Department of Infectious Diseases, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiran, Mexico City, Mexico; ³Laboratory of Clinical Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland; ⁴Experimental Transplantation and Immunology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland;

Abstract

We performed allogeneic hematopoietic stem cell transplantation in a patient with GATA2 deficiency and an Epstein-Barr Virus (EBV)-related spindle-cell tumor involving liver and possibly bone. He received a matched related donor transplant with donor peripheral blood stem cells following a myeloablative conditioning regimen. He achieved rapid and high levels of donor engraftment and had complete reversal of the clinical and immunologic phenotype of MonoMAC/GATA2 deficiency and eradication of the EBV tumors after 3 years of follow-up. Thus, allogeneic hematopoietic stem cell transplant results in reconstitution of immunologic function and cure of EBV-associated malignancy in MonoMAC/GATA2 deficiency.

Keywords

GATA2; Epstein-Barr Virus

INTRODUCTION

The indications for hematopoietic cell transplantation (HCT) for congenital immunodeficiencies continue to expand as new disease identification is enabled by whole exome sequencing.(1) As would be expected given the underlying indication for transplantation, this also expands the infectious complications present prior to transplantation. The outcomes of transplantation in the face of active infectious disease are an important field of study.

Corresponding Author: Dr. Mark Parta, 9000 Rockville Pike, Bldg.10/CRC, 3-3142, Bethesda, MD 20892, Tel: Fax:, mark.parta@nih.gov.

Conflict of Interest:

The authors declare that they have no conflict of interest.

Haploinsufficiency of GATA2, a transcription factor necessary for hematopoietic stem cell maintenance and development, results in multiple manifestations including: MonoMAC syndrome (monocytopenia with *Mycobacterium avium* complex [MAC] or non-tuberculous mycobacteria [NTM] infections); DCML (dendritic cell, monocyte and NK lymphocyte deficiency), familial myelodysplastic syndrome (MDS)/acute myelogenous leukemia (AML), and Emberger syndrome (lymphedema and myelodysplastic syndrome). The cytopenias (monocytes, B- and NK lymphocytes and dendritic cells) also result in fungal, bacterial, and viral infections, the latter including those due to human papillomavirus and Epstein-Barr virus (2, 3)

EBV viremia and smooth muscle tumors have been identified in a substantial number of GATA2-deficient patients.(4) In the original MonoMAC report, over 10% of patients developed persistent EBV infections or complications, including a posterior orbital leiomyosarcoma, which was excised prior to transplant. However, there was multifocal involvement at autopsy following complications from a matched related donor HCT for chronic myelomonocytic leukemia (CMML).(3)

Establishing therapies for EBV-related disease has presented an extraordinary challenge. The antagonism of viral replication by current drugs has not proven rewarding. Since the expression pattern of EBV proteins has been defined, these molecules have been studied as potential targets for immunotherapy.(5, 6) Unfortunately, the expression patterns of EBV genes in non-B cell malignancies and their relation to oncogenesis is not defined, nor is the presumption of a defect in EBV-specific immunity established. This leaves the question open as to the role of hematopoietic cell transplantation (HCT) in T-cell, NK-cell and mesenchymal EBV-associated tumors, which relies on graft-versus-tumor effect for its efficacy. These questions are relevant in the evolution of EBV-related disease in patients with GATA2 deficiency.

Hematopoietic cell transplantation (HCT) has been reported by our group for the treatment of GATA2 deficiency and severe infections (predominantly disseminated NTM).(7) We describe a young man with EBV-associated smooth muscle malignancy in the setting of GATA2 deficiency, and the correction of GATA2 deficiency and elimination of the EBV tumors with HCT.

PATIENTS AND METHODS

Patients

The patient underwent screening/evaluation under a protocol to study the natural history, genetics, phenotype and treatment of mycobacterial infections and allogeneic hematopoietic stem cell transplantation for patients with mutations in GATA2 or the MonoMAC syndrome. The studies were approved by the institutional review boards of the National Institute of Allergy and Infectious Diseases and the National Cancer Institutes, respectively, and were independently monitored for safety and data accuracy. Informed consent was obtained for all patients and donors in accordance with the Declaration of Helsinki. ([ClinicalTrials.gov](https://clinicaltrials.gov) number, NCT00923364). The inclusion and donor selection criteria are previously described.(7)

Supportive care

We followed standard guidelines for supportive care established at the National Institutes of Health Clinical Research Center (NIH CC) for patients undergoing allogeneic HCT.

Flow cytometry

CD14+ monocytes, CD3+/CD56+ NK cells, CD19+ B lymphocytes, and CD3+ T lymphocytes were quantified by flow cytometry pre-HSCT and at designated intervals post-HSCT.

EBV

EBV quantitation was performed on EDTA whole blood. The test was developed and performance characteristics determined by the Department of Laboratory Medicine, NIH and has not been cleared or approved by the USFDA. Reported units of copies/mL were calibrated to International Units (IU)/mL beginning October 2014.

Analysis of chimerism

Engraftment of donor cells was assessed using polymorphisms in regions known to contain short tandem repeats. Peripheral blood CD14+, CD3+/CD56+, CD19+ and CD3+ cells were selected using flow cytometry at the designated time points, and chimerism was assessed on these subpopulations. In addition, CD14+/CD15+ myeloid cells and CD3+ T lymphocytes were selected using immunobeads, and chimerism was assessed on the selected cells. The lower limit of sensitivity for this method is 1%–3% of donor-type polymorphic markers in the mixture; these sensitivities are on the basis of studies using mixtures of known proportions of allogeneic DNA samples.

Pathology

Pathology examination of hepatic tumors was performed with stains for smooth muscle actin, CD31, CD34, c-KIT, desmin and HHV-8. In situ hybridization for EBV was performed with EBER probe. Immunoperoxidase and in-situ hybridization were developed and their performance characteristics determined by the Laboratory of Pathology, NCI and are not FDA cleared or approved.

Molecular Pathology

Molecular pathology examination of bone marrow aspirates consisted of DNA extraction (PSS USA Magnatron System BLX automated DNA extraction robot) and PCR amplification for detection of immunoglobulin (IGH and IGk) and T-cell receptor gene (TRG locus) rearrangements.(8) Products were analyzed by capillary electrophoresis on an ABI 3130xl Genetic Analyzer and electropherograms analyzed using GeneMapper software version 4.0. Additional reactions were performed on the IGk locus using the Biomed II primer set. (9) Same analysis. IGH PCR is capable of detecting a clonal population comprising 2–10% of the B-cell population. For the TRG locus, PCR was performed as described. (10) These tests were developed and their performance characteristics determined by the Molecular Diagnostics Unit of the Laboratory of Pathology, NCI and have not been cleared or approved by the USFDA.

RESULTS:

Case Description

The patient is a 24 year old man, whose course antecedent to the development of an EBV-associated spindle cell tumor of the liver has been described (11). In brief, 6 years prior to transplantation he had immigrated to the United States from the Philippines, and in the same year had developed *Mycobacterium szulgai* lymphadenitis and pulmonary disease. He was successfully treated with combined surgical and medical therapy. He had recurrent otitis and pneumonias during childhood and persistent warts of the hands and feet. Six months prior to evaluation at the NIH CC he had new pulmonary and skin disease due to MAC. Initial hematologic evaluation revealed multilineage cytopenias (T, B and NK lymphocytes, monocytes and eventually neutrophils) and a hypocellular marrow. With a clinical phenotype consistent with the MonoMAC syndrome, mutation analysis of GATA2 demonstrated a single base transition, cDNA 1186 C>T causing a substitution of tryptophan codon for arginine at amino acid 396 (R396W). This mutation has been reported previously in GATA2 deficient patients. (12)

Computed tomography of the chest and abdomen, performed to assess the extent of remnant mycobacterial disease, revealed multiple enhancing lesions in the liver initially felt to be consistent with abscesses. An EBV serum PCR was positive at log 3.53. Needle biopsy of two liver lesions showed a well-circumscribed spindle cell neoplasm with a very low mitotic rate and no areas of necrosis. The hepatic parenchyma adjacent to the tumor showed mild inflammation but was otherwise normal. The tumor cells reacted with antibodies against smooth muscle actin and were negative for HHV-8, CD34 and CD31. In situ hybridization for EBV using the EBER probe was positive in all tumor cells but negative in the adjacent normal liver, consistent with an EBV-associated smooth muscle tumor (SMT).

He returned in six months later with intermittent back pain in the lower cervical and thoracic spine. This symptom had been evaluated 5 months previously, and no radiographic findings were present. Computed tomography of the chest abdomen and pelvis revealed stable hepatic lesions. However, MRI demonstrated multiple enhancing liver lesions, the largest of which was ~3cm in transaxial diameter and multiple enhancing lumbar and thoracic vertebral lesions. 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) of the torso demonstrated mediastinal and left hilar adenopathy, a splenic lesion, and 7–8 hepatic areas of hypermetabolism, the largest in the R tip inferiorly. There were scattered hypermetabolic skeletal lesions in thoracic vertebrae, the left scapula and right pelvis. (Figure 1)

Immediately prior to transplant his exam was significant for normal vital signs and a persistent wart on the right hand. He had mild tenderness of the spine with palpation. Laboratory evaluation was notable for pancytopenia (WBC 2.39 K/μl, Hgb 11.6 g/dl, platelets 71 K/μl, ANC 1100 K/μl, ALC 280 K/μl, AMC 0). There was hypoalbuminemia 3.3 g/dl (3.7–4.7) and elevation of alkaline phosphatase 197 U/L (37–116) and alanine aminotransferase 60 U/L (6–41). Whole blood PCR for EBV was 3.10 log10, and CMV, HHV6 and adenovirus PCRs were negative.

The peripheral blood smear showed mild polychromasia with macrocytosis, anisopoikilocytosis, with dacrocytes and fragmented red cells. There was moderate leukopenia, marked lymphocytopenia, and mild eosinophilia and thrombocytopenia. Bone marrow biopsy revealed a hypocellular marrow (30%) with no evidence of dysplasia or increased blasts, and GATA2-deficiency characteristic abundant megakaryocytes with hypolobation and abnormal separation of nuclear lobes, decreased peripheral blood monocytes and bone marrow CD20+ cells.

The patient underwent 10/10 HLA-matched sibling peripheral blood stem cell transplant. Conditioning for the HSCT consisted of fludarabine 40 mg/m² IV once daily for 4 days (–6 through –3), busulfan 3.2 mg/kg IV once daily for 4 days (–6 through –3). Adjustments to busulfan doses are based on a test dose administered 5–14 days prior to conditioning. On day 0 the patient received 5×10^6 CD34+ cell/kg of the recipient's body weight of granulocyte-colony stimulating factor (G-CSF) mobilized PBSCs from his EBV-CA IgG+ sister. Engraftment occurred on day 10 with whole blood chimerism 96% (CD3 66% and myeloid 100%) at 2 weeks and bone marrow 90% donor. The transplant was complicated by cutaneous graft-versus-host disease (GVHD) that was responsive to topical steroids. Post-transplant GVHD prophylaxis consisted of methotrexate 5 mg/m² IV on days +1, 3, 6 and 11 and tacrolimus daily from day –3 until day +180.

Immunophenotypes and EBV viremia through the post-transplant course are seen in Table 1. Reconstitution of NK cells preceded that of CD19+ cells. EBV viremia was assessed twice weekly through day 60 and weekly thereafter, and was suppressed immediately after transplant and only transiently reappeared at very low levels thereafter, with the 3 year followup viral load again undetectable. The patient's pain (primarily spinal) remitted soon after transplantation and he has remained asymptomatic since. Radiology, including MR of the liver and PET-CT scans of the torso, has demonstrated stability or involution of solid lesions and loss of PET enhancement in the liver, spleen and spinal lesions. (Figure 1).

Discussion

GATA2 deficiency predisposes to multiple infectious and malignant sequelae, including those related to EBV infection. Solid tumors of mesenchymal cell origin are associated with EBV, as described in the original MonoMAC report.(13–15) Other immunodeficient states, including HIV infection, immunosuppression after solid organ transplant, and congenital immunodeficiencies are also predisposing factors to these tumors.(16–20) We have used HSCT successfully in GATA2-deficient patients to correct immunodeficiencies leading to mycobacterial and viral infections, and to correct myelodysplastic syndromes and high-risk cytogenetic abnormalities. However, this is the first report of reversal of an EBV-associated smooth muscle tumor with HSCT in a patient with GATA2 deficiency.

Current therapies for EBV-related disease most often include decreasing iatrogenic immunosuppression and using monoclonal antibodies that target the major hematopoietic reservoir of EBV, CD20+ B-lymphocytes.(21) Since evidence supports the independent infection of smooth muscle cells, we did not believe that this approach would be sufficient, despite its use in conjunction with surgical resection and a reduction in immunosuppression

in one report.(22, 23) Anti-viral therapies have not been shown to have a role in the treatment of any condition associated with EBV, perhaps because the oncogenic role of EBV is not dependent on independent viral replication. EBV-targeted cellular therapies have gained acceptance for the treatment of post-transplant lymphoproliferative disease, but the expression of EBV antigens in smooth muscle tumors differs from that seen in lymphoproliferative EBV tumors, suggesting that this approach might not be successful in this patient.(24) Radiation therapy, doxorubicin in combination with olaratumab, and many other chemotherapeutic regimens have been used to treat soft-tissue sarcomas with variable success.(25) Substitution of sirolimus for other immunosuppressants may have contributed to regression of a hepatic tumor in a kidney-transplant recipient.(26)

We have previously reported on outcomes associated with HSCT for GATA2 deficiency. (7) The current case represents successful transplantation and repair of immune defects as evidenced by normalization of cell counts, marrow findings, and absence of recurrence of sentinel infections or new infections consistent with the immunodeficiency. We used radiology, nuclear medicine, chemistry and virologic studies to establish and follow the disease in our patient. MR of the abdomen demonstrated stable or regressing lesions at 3 years, and serial PET-CTs post-transplantation revealed normalization of previously involved sites, including bone, spleen and liver lesions. We do not have pathologic confirmation to establish the etiology of all of the PET-avid lesions in the spine prior to transplant. However, the frequent multi-focal disease and association with vascular smooth muscle cells in previous reports of EBV-related smooth muscle tumors is consistent with the PET finding. Alternatively, our patient had had multifocal disease with two mycobacterial infections, but these never required clinical consideration in the immediate pre-transplant or transplant course.(27)

We did not systematically assess immunity to EBV pre-transplant, relying instead on a global assessment of immunodeficiency as represented by cytopenias, and are thus unable to compare the restoration of immunity in a virus-specific fashion. Because of the nature and anatomy of the smooth muscle tumor, we are dependent on comparisons of size and PET avidity to presume regression and cure. Nevertheless, we have demonstrated that HSCT to reverse the immunodeficiency associated with GATA2 deficiency provides a durable control of an EBV-related smooth muscle malignancy after three years of follow-up.

Acknowledgments

This project has been funded in whole or in part with federal funds from the National Cancer Institute, National Institutes of Health, under Contract No. HHSN261200800001E. The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government. This research was supported by the Intramural Research Program of the NIH, National Cancer Institute, Center for Cancer Research and by the National Institute of Allergy and Infectious Diseases.

REFERENCES

1. Chinen J, Notarangelo LD, Shearer WT. Advances in basic and clinical immunology in 2014. *J Allergy Clin Immunol*. 2015;135(5):1132–41. [PubMed: 25956014]

2. Mace EM, Hsu AP, Monaco-Shawver L, Makedonas G, Rosen JB, Dropulic L, et al. Mutations in GATA2 cause human NK cell deficiency with specific loss of the CD56(bright) subset. *Blood*. 2013;121(14):2669–77. [PubMed: 23365458]
3. Vinh DC, Patel SY, Uzel G, Anderson VL, Freeman AF, Olivier KN, et al. Autosomal dominant and sporadic monocytopenia with susceptibility to mycobacteria, fungi, papillomaviruses, and myelodysplasia. *Blood*. 2010;115(8):1519–29. [PubMed: 20040766]
4. Cohen JI, Dropulic L, Hsu AP, Zerbe CS, Krogmann T, Dowdell K, et al. Association of GATA2 Deficiency With Severe Primary Epstein-Barr Virus (EBV) Infection and EBV-associated Cancers. *Clin Infect Dis*. 2016;63(1):41–7. [PubMed: 27169477]
5. Young L, Alfieri C, Hennessy K, Evans H, O'Hara C, Anderson KC, et al. Expression of Epstein-Barr virus transformation-associated genes in tissues of patients with EBV lymphoproliferative disease. *N Engl J Med*. 1989;321(16):1080–5. [PubMed: 2552313]
6. Rooney CM, Smith CA, Ng CY, Loftin SK, Sixbey JW, Gan Y, et al. Infusion of cytotoxic T cells for the prevention and treatment of Epstein-Barr virus-induced lymphoma in allogeneic transplant recipients. *Blood*. 1998;92(5):1549–55. [PubMed: 9716582]
7. Cuellar-Rodriguez J, Gea-Banacloche J, Freeman AF, Hsu AP, Zerbe CS, Calvo KR, et al. Successful allogeneic hematopoietic stem cell transplantation for GATA2 deficiency. *Blood*. 2011;118(13):3715–20. [PubMed: 21816832]
8. Ramasamy I, Brisco M, Morley A. Improved PCR method for detecting monoclonal immunoglobulin heavy chain rearrangement in B cell neoplasms. *J Clin Pathol*. 1992;45(9):770–5. [PubMed: 1401205]
9. van Dongen JJ, Langerak AW, Bruggemann M, Evans PA, Hummel M, Lavender FL, et al. Design and standardization of PCR primers and protocols for detection of clonal immunoglobulin and T-cell receptor gene recombinations in suspect lymphoproliferations: report of the BIOMED-2 Concerted Action BMH4-CT98–3936. *Leukemia*. 2003;17(12):2257–317. [PubMed: 14671650]
10. Lawnicki LC, Rubocki RJ, Chan WC, Lytle DM, Greiner TC. The distribution of gene segments in T-cell receptor gamma gene rearrangements demonstrates the need for multiple primer sets. *J Mol Diagn*. 2003;5(2):82–7. [PubMed: 12707372]
11. Camargo JF, Lobo SA, Hsu AP, Zerbe CS, Wormser GP, Holland SM. MonoMAC syndrome in a patient with a GATA2 mutation: case report and review of the literature. *Clin Infect Dis*. 2013;57(5):697–9. [PubMed: 23728141]
12. Hsu AP, Sampaio EP, Khan J, Calvo KR, Lemieux JE, Patel SY, et al. Mutations in GATA2 are associated with the autosomal dominant and sporadic monocytopenia and mycobacterial infection (MonoMAC) syndrome. *Blood*. 2011;118(10):2653–5. [PubMed: 21670465]
13. Spinner MA, Sanchez LA, Hsu AP, Shaw PA, Zerbe CS, Calvo KR, et al. GATA2 deficiency: a protean disorder of hematopoiesis, lymphatics, and immunity. *Blood*. 2014;123(6):809–21. [PubMed: 24227816]
14. Baumforth KR, Young LS, Flavell KJ, Constandinou C, Murray PG. The Epstein-Barr virus and its association with human cancers. *Mol Pathol*. 1999;52(6):307–22. [PubMed: 10748864]
15. Schubach WH, Hackman R, Neiman PE, Miller G, Thomas ED. A monoclonal immunoblastic sarcoma in donor cells bearing Epstein-Barr virus genomes following allogeneic marrow grafting for acute lymphoblastic leukemia. *Blood*. 1982;60(1):180–7. [PubMed: 6282364]
16. Moore Dalal K, Antonescu CR, Dematteo RP, Maki RG. EBV-Associated Smooth Muscle Neoplasms: Solid Tumors Arising in the Presence of Immunosuppression and Autoimmune Diseases. *Sarcoma*. 2008;2008:859407. [PubMed: 19079588]
17. Al Hussain T, Haleem A, Alsaad KO. Synchronous hepatic, mesenteric and pulmonary Epstein-Barr virus-associated smooth muscle tumors in a renal transplant recipient. *Clin Transplant*. 2010;24(5):579–84. [PubMed: 20156224]
18. Cheuk W, Li PC, Chan JK. Epstein-Barr virus-associated smooth muscle tumour: a distinctive mesenchymal tumour of immunocompromised individuals. *Pathology* 2002;34(3):245–9. [PubMed: 12109785]
19. McClain KL, Leach CT, Jenson HB, Joshi VV, Pollock BH, Parmley RT, et al. Association of Epstein-Barr virus with leiomyosarcomas in children with AIDS. *N Engl J Med*. 1995;332(1):12–8. [PubMed: 7990860]

20. Lee ES, Locker J, Nalesnik M, Reyes J, Jaffe R, Alashari M, et al. The association of Epstein-Barr virus with smooth-muscle tumors occurring after organ transplantation. *N Engl J Med*. 1995;332(1):19–25. [PubMed: 7990861]
21. Dierickx D, Tousseyn T, Gheysens O. How I treat posttransplant lymphoproliferative disorders. *Blood*. 2015;126(20):2274–83. [PubMed: 26384356]
22. Jenson HB, Montalvo EA, McClain KL, Ench Y, Heard P, Christy BA, et al. Characterization of natural Epstein-Barr virus infection and replication in smooth muscle cells from a leiomyosarcoma. *J Med Virol*. 1999;57(1):36–46. [PubMed: 9890420]
23. Jericho H, Weinstein J, Melin-Aldana H, Leuer KC, Wyers M, Alonso EM, et al. Successful treatment with rituximab of an Epstein-Barr virus-associated leiomyosarcoma occurring after liver transplantation. *J Pediatr Gastroenterol Nutr*. 2014;58(1):e2–4. [PubMed: 24378523]
24. Petrilli G, Lorenzi L, Paracchini R, Ubiali A, Schumacher RF, Cabassa P, et al. Epstein-Barr virus-associated adrenal smooth muscle tumors and disseminated diffuse large B-cell lymphoma in a child with common variable immunodeficiency: a case report and review of the literature. *Int J Surg Pathol*. 2014;22(8):712–21. [PubMed: 21454372]
25. Tap WD, Jones RL, Van Tine BA, Chmielowski B, Elias AD, Adkins D, et al. Olaratumab and doxorubicin versus doxorubicin alone for treatment of soft-tissue sarcoma: an open-label phase 1b and randomised phase 2 trial. *Lancet*. 2016;388(10043):488–97. [PubMed: 27291997]
26. Tan CS, Loh HL, Foo MW, Choong LH, Wong KS, Kee TY. Epstein-Barr virus-associated smooth muscle tumors after kidney transplantation: treatment and outcomes in a single center. *Clin Transplant*. 2013;27(4):E462–8. [PubMed: 23682851]
27. Deyrup AT, Lee VK, Hill CE, Cheuk W, Toh HC, Kesavan S, et al. Epstein-Barr virus-associated smooth muscle tumors are distinctive mesenchymal tumors reflecting multiple infection events: a clinicopathologic and molecular analysis of 29 tumors from 19 patients. *Am J Surg Pathol*. 2006;30(1):75–82. [PubMed: 16330945]

Key Points

- Allogeneic transplant for EBV Malignancies
- Correction of EBV Malignancies

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

FIG 1.

A. MRI liver, demonstrating an enhancing lesion (arrow). B. PET CT image with enhancing lesions in the liver (arrow), spleen, and cervical spine (arrow). C. H&E stained section of the tumor (400x) D. Positive staining with antibody to smooth muscle actin (400x) E. Positive in-situ hybridization for EBV (400x) F. PET, 2 years post-transplant with resolution of enhancement.

Table 1.

Immunophenotype/chimerism and EBV whole blood viremia through year 3 post-transplant

	pretransplant	Day 103	Day 364	Day 728	Day 1298	Normal range
CD3%/chimerism	99.3	62.6/88	50.7/100	51.8/100	58.7/100	60–83.7
CD3#/μl	311	680	756	1274	1925	714–2266
CD4/CD3%	50.2	31.5	27.2	28.7	31.2	31.9–62.2
CD4/CD3#	159	342	416	706	1023	359–1565
CD8/CD3%	44.8	29.6	21	21.5	24.5	11.2–34.8
CD8/CD3#	142	322	321	529	804	178–853
CD19%/Chimerism	0.2	19.4/100	40.7/100	41.2/100	35.6/100	3.3–19.3
CD19#	0	210	592	1014	1168	61–321
NK %/chimerism	0.2	15.4/100	6.5/100	5.9/100	5.6/100	6.2–34.6
NK#	1	167	95	145	184	126–729
Myeloid chimerism		99	99	100	100	100
EBV log10	3.53	undetectable	undetectable	2.55	undetectable	