lymphoid and myeloid cells compared to their MSD. Additionally, increased tissue expression of PI GF by IHC was seen in skin biopsies of aGVHD, while GI aGVHD tissue demonstrated pathologically low PI GF expression. To our knowledge, these results provide the first evidence of altered circulating and tissue expression of PI GF occurring in the HCT setting. Studies are ongoing to determine the role of PI GF in neovascularization and tissue repair in aGVHD, and on the direct angiogenic and immune regulatory effect of PI GF in HCT.

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Viral Infections after Umbilical Cord Blood Transplant: A Retrospective Analysis of 156 Children Transplanted at a Single Institution
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Umbilical cord blood (UCB) is an alternative option for hematopoietic stem cell transplantation and it has been successfully used to treat children with malignant and non-malignant diseases. The slower rate of neutrophil engraftment and delayed immune reconstitution impose a substantial risk for infections and mortality. Furthermore, the use of anti-thymocyte globulin (ATG) has been linked to a substantial risk for infections and mortality. Furthermore, the use of anti-thymocyte globulin (ATG) has been linked to a substantial risk for infections and mortality. Currently, close PCR surveillance allows early detection of viremia and aggressive treatment.

Paradoxical Effect of Donor Cytomegalovirus (CMV) Status on CMV Reactivation after T-Cell Depleted (TCD) Stem Cell Transplantation (SCT)
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Background: CMV recipient seropositivity (R+) is a predictor for CMV viremia after SCT. Cytotoxic T-lymphocytes (CTL) are critical for CMV immunity. Conventional allografts from CMV seropositive donors (D+) confer some CMV immunity though transfer of donor CTLs to the recipient. Thus for CMV R+, CMV D+ are preferentially chosen over CMV D-. In contrast, ex-vivo T-cell depleted (TCD) allografts are deficient in CMV CTLs. The effect of donor serostatus on CMV reactivation has not been examined after TCD SCT. We studied the effect of CMV donor serostatus on the incidence of CMV viremia in a cohort of adult CMV R+, TCD SCT monitored by CMV PCR and treated preemptively.

Methods: CMV R+ adults with hematologic malignancies who received peripheral blood CD34+ selected allografts after myeloablative conditioning regimens from March 1, 2010 through May 2013 were monitored prospectively by CMV PCR at least weekly from day (d) +14 through +100 and at least once every 2 weeks through d +180. Preemptive therapy was initiated for CMV viremia, defined as ≥ 1 positive PCR value. There was no CMV prophylaxis during the study period. Follow up was through May 31, 2014. Time-dependent Cox-proportional hazard model of univariate and multivariate stepwise selection analyses were performed to identify predictors of CMV viremia.

Results: Of 113 CMV R+ (median age 57.6 years, 22.5-73.0), 60 (53%) had acute leukemia, 23 (20%) myelodysplastic syndrome, 18 (16%) multiple myeloma and 12 (11%) other. Donors were 48 (42%) matched-related (MRD), 45 (40%) matched unrelated (MUD), or 20 (18%) mismatched; 68 (60%) CMV D+ or 45 (40%) D-. The cumulative incidence of CMV viremia at 6 months was 79%. Time to onset of viremia was median 26 days (13-83) after SCT, and time to resolution of viremia a median 30.5 days from onset of viremia. The incidence of CMV viremia was higher in R+/D+ compared to R+/D− (90.5% versus 62.2%; P=0.001). The median time to onset and to resolution for R+/D+ vs R+/D− were not significantly different. In multivariable analysis, R+/D− pts were at lower risk for CMV viremia compared to R+/D+ (HR: 0.57, 95% CI: 0.36-0.90; P=0.017). In contrast, multiple myeloma (HR: 2.22, 95% CI: 1.24-3.98; P=0.008) was associated with increased risk compared with acute leukemia. Having a mismatched donor was also associated with increased risk for CMV viremia per se was not associated with a high mortality.

Conclusion: We observed a high prevalence of viral infections among UCB recipients and a positive association of its occurrence with HLA-mismatch, development of acute or chronic GVHD and the use of ATG. Viral infections were usually associated with other infectious agents such bacteria or fungi and this could be an important factor for morbidity and mortality. Currently, close PCR surveillance allows early detection of viremia and aggressive treatment.
Cluster of Fulminant Toxoplasmosis in T-Cell Depleted (TCD) and Cord Blood (CB) Stem Cell Transplant (SCT) Recipients: Impact of Aggressive Prophylaxis and Routine Monitoring By Toxoplasma PCR for High Risk Patients

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Background: Fulminant disseminated toxoplasmosis (FTX) is a rare complication of allogeneic SCT with an incidence ranging from 1–8% based on endemicity. Plasma quantitative PCR (qPCR) affords rapid diagnosis. Before 2011, patients (pts) at MSK received pre-SCT TMP/SMZ (T/S) for Pneumocystis (PCP) prophylaxis (ppx). Pts with positive (+) toxo IgG (R+) or from + donors (D+) received Atovaquone (ATQ) ppx starting on d +30-50 post SCT. The incidence of toxo IgG. PPX: In Period A, R+ or D+ received ATQ ppx starting on d +30-50 post-SCT with no routine qPCR monitoring. In Period B, R+ or D+ received ATQ ppx starting day (d) 30-50 post SCT. The incidence of toxo IgG was 0-1 cases/year. In 2011, T/S ppx pre-SCT was limited to pts at high risk for PCP. From January through June 2013 we observed a cluster of 4 cases of FTX. Since July 2013, we have, therefore, implemented “aggressive” ppx.

Methods: We compared the incidence of FTX in adult recipients of peripheral blood CD34+ selected (TCD) or CB allografts for hematologic malignancies from May 2012 through June 2013 (Period A) and from July 2013 through August 2014 (Period B). R+ includes positive or equivocal toxo IgG. PXPX: In Period A, R+ or D+ received Atovaquone (ATQ) ppx starting on d +30-50 post-SCT with no routine qPCR monitoring. In Period B “aggressive” ppx consisted of T/S pre-SCT and ATQ starting on d +14. qPCR was checked at least weekly from d+14 to 60 and as needed thereafter. In Periods A and B, qPCR was ordered in symptomatic pts at clinician’s discretion. FTX cases are defined as positive qPCR with fulminant course and no alternative explanation.

Results: During Period A, 154 (114 TCD, 40 CB) pts had SCT including 19 (12.3%) R+. During Period B, 144 (118 TCD, 26 CB) pts had a SCT including 20 (13.9%) R+. In Period A, 4/154 (2.6%) pts had FTX vs. 0/144 (0%) pts in Period B. In period A, 3/19 (15.8%) R+ and 1 R-/D- pt had FTX. R+ cases came from Turkey, Ukraine and West Africa, received TCD (2) or CB (1) transplants from D- (3) for acute leukemia (2) or multiple myeloma (1) and were diagnosed <60 days post SCT. The fourth case was R-/D-, presented 5 months after SCT, after traveling to UK and Mexico. Three pts presented with high fevers and 1 with multi-system deterioration. All pts progressed to multi-organ failure and expired within 7 days of presentation. At death qPCR ranged 0.3-5.0x10^6 copies/ml. No autopsies were done. An investigation for a shared nosocomial source was unrevealing. During Period B, 1/20 (5%) R+ had 2 positive qPCRs. This pt was asymptomatic and noncompliant with ATQ ppx. He was treated with T/S and subsequent PCRs were negative. The diagnostic yield of qPCR was 0.76% (2 positives out of 264 qPCR performed).

Conclusions: 1) Toxoplasmosis infection should be immediately considered in zero-positive TCD and CB SCT pts presenting with fevers of unknown source. 2) We advocate early and aggressive ppx in sero-positive patients. 3) Routine monitoring with qPCR should be strongly considered if noncompliance or suboptimal absorption with ppx is suspected. 4) Optimal preventive strategies for toxoplasmosis have to be determined for each Center based on the patient population.