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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 day (d) 30-50 post SCT. The incidence of toxoplasmosis 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. PPX: In Period A, R+ or D+ received ATQ ppx starting 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 post 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 0.3-5.0x106 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 positive 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 seropositive 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.

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The Relationship Between Pre-Transplant 25-Hydroxy-Vitamin D Levels, Survival and Graft-Versus-Host Disease, in Allogeneic Haematopoietic Stem Cell Transplantation
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Background/Aim: Low serum vitamin D levels are becoming increasingly implicated in infections, pulmonary disorders, cancer incidence and autoimmune conditions. Their role in allogeneic haematopoietic stem cell transplantation (alloHSCT) remains unclear, with some studies showing deficiency to be associated with lower overall survival (OS) and increased graft versus host disease (GVHD) rates, while other studies show no differences in OS or GVHD rates. We investigated the relationship between low vitamin D levels pre-alloHSCT and post-transplant outcomes (OS, progression-free survival [PFS], non-relapse mortality [NRM], relapse and acute and chronic GVHD).

Methods: We reviewed 492 alloHSCT recipients who had pre-alloHSCT and post-transplant outcomes (OS, progression-free survival [PFS], non-relapse mortality [NRM], relapse and acute and chronic GVHD).

Results: The vitamin D deficient cohort had a higher mortality rate compared to the replete group. This reduction in survival was maintained in the multivariate analysis (HR 1.5, 95% CI 1.1-2.0, P=0.013). There were no significant differences in NRM, PFS, acute/chronic GVHD, or relapse rates between the two groups. No significant differences were noted with any of these outcomes in the 123 B-NHL patients. There was no association between 25-OH-Vit D levels and DRI.

Conclusions: Vitamin D deficiency appears associated with increased mortality in alloHSCT recipients. The mechanisms of this finding remain unclear. GVHD rates did not appear to be affected by deficiency. Further research looking at whether immunomodulatory effects of vitamin D are responsible for the survival differences noted in our study, and previously reported studies, is required.