data suggests that a CSA trough level less than 125 ng/ml on day 0 is not predictive of acute or chronic GVHD.

223

ASSESSMENT OF LUNG FUNCTION BEFORE AND AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN A SINGLE PEDIATRIC CENTER

Quigg, T.C.[1], Kim, Y.-J.[3], Goebel, W.S.[2], Spiegel, C.B.[2], Haut, P.R.[2]
[1] Riley Hospital for Children-Indiana University School of Medicine, Indianapolis, IN; [2] Riley Hospital for Children-Indiana University School of Medicine, Indianapolis, IN; [3] Riley Hospital for Children-Indiana University School of Medicine, Indianapolis, IN

Background: Allogeneic hematopoietic stem cell transplantation (aHSCT) is being used with increasing success in pediatric patients to treat a variety of malignant and non-malignant diseases. However, pulmonary complications account for meaningful morbidity and mortality in aHSCT recipients.

Objective: We assessed the prevalence of pre and post-aHSCT lung function abnormalities at Riley Hospital for Children to identify risk factors that may predict post-aHSCT morbidity and mortality.

Methods: We retrospectively reviewed the medical records of 46 patients, aged 5–21 years, who received aHSCT between 1 January 2001 and 31 December 2006. Forty-one patients, who underwent pulmonary function tests (PFTs) both before and after aHSCT, were eligible for analysis. Pertinent demographic, aHSCT and treatment-related data, and baseline (pre-aHSCT), 1 and 2-year post-aHSCT PFT data were collected. Forced expiratory volume in 1 second ($FEV_{1)}$, forced vital capacity (FVC), residual volume (RV), total lung capacity (TLC), and diffusion capacity for carbon monoxide adjusted for alveolar volume and hemoglobin (DL_{COa}/VA) were determined as percentage predicted for age, sex, and length matched controls. Analyses included logistic regression, with and without generalized estimating equations, and mixed effects models.

Results: Significantly lower $FEV_{1,}$ FVC, TLC, but similar FEV_1/FVC was noted at 1 year post-aHSCT. However, these findings were no longer significant at 2 years post-aHSCT. Low baseline DL_{COa}/VA was associated with death. Refractory disease before aHSCT was significantly associated with lower FEV_1, FVC, and TLC after aHSCT. Age, CMV status, previous pulmonary-toxic chemotherapy, and aHSCT conditioning were not significantly associated with outcomes. Acute and chronic graft versus host disease (GVHD) was significantly associated with higher post-aHSCT RV.

Conclusions: Obstructive lung patterns contribute to post-aHSCT morbidity, especially in the first year following aHSCT. Low baseline DL_{COa}/VA was a risk factor for mortality. Pediatric patients who have evidence of acute and chronic GVHD are more likely to have associated obstructive lung disease which suggests that therapeutic intervention may prevent morbidity. Further prospective studies are needed to assess the utility of long-term respiratory monitoring in pediatric aHSCT recipients.

224

MATCHED UNRELATED BONE MARROW TRANSPLANT FOR OMENN SYNDROME

Nahum, A., Reid, B., Grunebaum, E., Roifman, C.M. The Hospital for Sick Children

Little information is currently available on the outcome and the long term restoration of immune function in infants with Omenn syndrome (OS) treated with bone marrow transplantation (BMT). We prospectively followed patients with OS who received matched unrelated donor bone marrow transplantation at our center. Engraftment, immune reconstitution and transplant-related complications were recorded. Humoral and cellular immunity were evaluated. Six patients with OS were diagnosed at a mean age of 4.6 months. Two had mutations in the RMRP gene, one had mutations in DNA Ligase 4, while the rest genotype could not be determined. They received a matched unrelated donor bone marrow transplantation as the first BMT at the mean age of 9.4 months. All six patients are alive and well at a mean 95 months after transplant. All patients have evidence of full hemopoetic engraftment and robust immune reconstitution. Three out of six patients developed GvHD of Grade II or more, which was reversed in all patients by using short courses of high dose methylprednisolone. We have shown here that matched unrelated donor bone marrow transplantation is highly effective in curing patients with Omenn syndrome regardless of their genotype. This mode of treatment should be preferred for patients with OS when a related identical donor is not available.

225

RELATIONSHIP BETWEEN ACETAMINOPHEN DOSAGE AND DEVELOPMENT OF ORGAN DYSFUNCTION DURING PEDIATRIC HEMATOPOETIC STEM CELL TRANSPLANT

McArthur, J.A.[1], Mikhailov, T.[1], Rothchild, C.[1], Talano, J.A.[2] [1] Medical College of Wisconsin, Milwaukee, WI; [2] Medical College of Wisconsin, Milwaukee, WI

Background: Patients undergoing chemotherapy and radiation have been shown to be in a state of oxidative stress. Acetaminophen is known to cause depletion of glutathione, a key component of the body's antioxidant defense mechanism. Acetaminophen is also known to cause liver toxicity and recently has been linked with severity of lung disease in asthmatics and alcoholics. Therefore, we questioned whether acetaminophen usage in patients undergoing hematopoetic stem cell transplant (HSCT) could place them at risk for organ dysfunction.

Methods: A retrospective chart review was performed on all patients undergoing HSCT at the Children's Hospital of Wisconsin between January 1, 1995–January 1, 2005. Cumulative dosage of acetaminophen in mg/ kg was calculated on all patients during conditioning and the first 14 days after stem cell infusion. Charts were reviewed for evidence of veno-occlusive disease (VOD) of the liver as diagnosed by the attending HSCT physician, respiratory insufficiency as defined by requirement of ≥2 l/min of nasal cannula oxygen, and renal insufficiency as defined by doubling of the serum creatinine. Statistical analysis was done using the unpaired student t-test.

Results: Preliminary analysis found 330 patients who underwent HSCT during the study time period. There was a statistically significant difference in the mean acetaminophen dose used in patient who developed VOD (303 mg/kg) in comparison to those who did not (213 mg/kg) with $p = .036$. The difference in acetaminophen dosage between those who developed renal insufficiency (278mg/kg) compared to those who did not (210 mg/kg) was also significant ($p = .028$). The most significant difference was seen when comparing patients who did (277 mg/kg) and did not (202 mg/kg) develop respiratory insufficiency ($p = .0019$). Also of interest in our data set was that of the 80 patients who developed respiratory insufficiency (requirement of ≥2 l/min nasal cannula oxygen), 55 (69%) went on to require some form of mechanical ventilation. The relative risk of death in this population was 2.04 (95% CI 1.70–2.45).

Conclusion: This patient population is highly complex with multiple confounding variables. It is still unclear if acetaminophen is a cause or marker of severity of illness in pediatric HSCT patients. However, avoidance of frequent acetaminophen dosing may be beneficial whenever possible.

226

T-CELLS REDIRECTED AGAINST NKG2D-LIGANDS FOR THE IMMUNOTHERAPY OF OSTEOSARCOMA

Kakarla, S.[1,2], Shaffer, D.[1,2], Ahmed, N.[1,2], Wang, L.L.[2], Lee, D.A.[3], Sentman, C.L.[4], Gottschalk, S.[1,2] [1] Baylor College of Medicine, Houston, TX; [2] Baylor College of Medicine, Houston, TX; [3] University of Texas, MD Anderson Cancer Center, Houston, TX; [4] Dartmouth Medical School, Lebanon, NH

Background: Osteosarcoma is the most common pediatric bone tumor. Despite aggressive multimodal therapy survival rates for patients with metastatic or recurrent disease remain poor. New