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**PROSPECTIVE STUDY USING R2 MRI DEMONSTRATES HIGH IRON BURDEN IN ALLOGENEIC PEDIATRIC STEM CELL TRANSPLANT RECIPIENTS**

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**Background:** Iron overload has been implicated as a key co-morbid factor in post-stem cell transplant (SCT) outcomes. Quantifying iron burden has been a challenge as serum iron markers are imprecise. MRI is a relatively new and non-invasive tool that more accurately measures iron burden. We conducted a prospective study using MRI to assess iron burden in children undergoing SCT.

**Objective:** To determine the prevalence of iron overload using R2 MRI of the liver in a pediatric allo SCT population both pre and post-SCT. Relationships between excess iron and adverse outcomes such as graft vs. host disease (GVHD), infection, and death were secondary objectives.

**Methods:** Children  $\geq 5$  years old undergoing an allo SCT at Children's Hospital Boston from 2007-2009 were eligible for this study. Iron overload was defined as a liver iron concentration  $\geq 1.5$  mg iron/g dry liver tissue. A paired t-test was conducted with  $\alpha = 0.05$  to compare iron load at the two specified time points. A two-sample two-sided t-test was conducted at each time point for association with risk factors described above with  $\alpha = 0.1$ . This study was IRB approved.

**Results:** Twenty-eight patients were enrolled. The most common diagnoses were Pre-B ALL (N = 7), AML (N = 6), and aplastic anemia (N = 5). Pre-SCT, 82% (95% CI: 66% - 98%) of patients had iron overload by R2 MRI. At day 100 post-SCT, 95% (95% CI: 65% - 100%) had iron overload. The mean iron concentration ( $\pm$  std error) was  $4.97 \pm 3.54$  mg/g dwl liver at pre-SCT and  $7.55 \pm 4.37$  mg/g dwl liver at day 100 post-SCT. The day 100 post-SCT mean value was significantly higher than the mean value at pre-SCT (2.15 mg/g dwl liver,  $p < 0.0001$ ). For patients who developed an infection during the post-SCT period, the mean iron concentration, compared to patients who did not develop an infection, was significantly higher at pre-SCT and at day 100 post-SCT ( $p = 0.029$  and  $p = 0.0055$ , respectively). There was no statistically significant difference in iron concentration between patients who developed GVHD or died and those who did not.

**Conclusions:** We found that a high proportion of pediatric allo SCT patients have iron overload pre-SCT. In addition, there is a statistically significant rise in iron post-SCT ( $p < 0.0001$ ) and an association with increased incidence of infection in patients with elevated iron. Larger multi-center studies should be conducted to further examine the consequences of iron overload and evaluate potential interventions in this patient population.

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**ALEMTUZUMAB IS AN EFFECTIVE SALVAGE AGENT FOR REFRACTORY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS**

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**Background:** Familial hemophagocytic lymphohistiocytosis (FHLH) consists of several genetic disorders that compromise lymphocyte cytotoxicity and lead to the life-threatening hyper-inflammatory syndrome of HLH. Even with current standard HLH therapy, only approximately half of patients will experience complete resolution of disease, and mortality prior to allogeneic hematopoietic cell transplantation (HCT) remains a significant problem. Salvage therapies have been described only in limited case reports, and there are no large studies of second-line therapies.

**Methods:** We reviewed the charts of 22 pediatric and adult patients who received alemtuzumab for the treatment of refractory primary

HLH at our center or in consultation with our group. Patients had received conventional therapies for a median of 8 weeks (range 2-70) prior to alemtuzumab, and treatment immediately prior to alemtuzumab included dexamethasone (100%), etoposide (77%), cyclosporine (36%), intrathecal hydrocortisone+/-methotrexate (23%), methylprednisolone (9%), and rituximab (14%). Patients received a median dose of 1mg/kg alemtuzumab (range 0.1-8.9mg/kg) divided over a median of 4 days (range 2-10).

**Results:** Nineteen patients (86%) experienced a partial response. Seventeen patients (77%) survived to undergo allogeneic HCT at a median of 52 days following first alemtuzumab administration (range 16-121 days). One additional patient is surviving and not currently a candidate for HCT. Patients experienced an acceptable spectrum of complications, including CMV and adenovirus viremia. All but 1 patient undergoing HCT survived to day +100 following HCT.

**Conclusion:** Alemtuzumab is an effective salvage agent for refractory HLH, leading to disease improvement and survival to HCT in the majority of patients.

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**HIGH-DOSE CHEMOTHERAPY AND AUTOLOGOUS HEMATOPOIETIC STEM CELL RESCUE FOR CHILDREN WITH HIGH-RISK NEUROBLASTOMA. EXPERIENCE OF A SINGLE PEDIATRIC CENTER IN BOGOTÁ, COLOMBIA**

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Neuroblastoma (NB) is the most common extracranial solid tumor in children. Prognosis of high risk NB is extremely poor. The use of high-dose chemotherapy with autologous hematopoietic stem cell rescue in consolidation has resulted in improvements in survival and appears to have the largest impact on the survival of the high risk subset of patients although long-term event-free survival remains less than 40-50%. The aim of this retrospective study was to analyze the outcome of children with high-risk neuroblastoma who underwent Autologous Stem Cell Transplantation (ASCT) in a new pediatric stem cell transplant facility.

**Patients and Methods:** Between August 2008 to July 2011, 16 children underwent ASCT as part of a multimodality treatment approach consisted in induction chemotherapy, surgery, HDC and autologous stem cell rescue, radiotherapy and maintenance therapy with 13-cis retinoid acid. The conditioning regimen used in all cases consisted of Carboplatin (375 mg/m<sup>2</sup> for 4 days), Etoposide (300 mg/m<sup>2</sup> for 4 days), and Melphalan (60 mg/m<sup>2</sup> for 3 days).

**Results:** There were 16 patients with NB consisting of 6 males and 10 females. The median age was 4.7 years (range 1-14 years). The median weight was 17,4kg (range 8-40kg). 12 patients had stage IV-NB and 4 had high-risk stage III-NB. The source of stem cells was peripheral blood in 15 patients and bone marrow in 1 patient. The median time to Absolute Neutrophil Count  $> 0.5 \times 10^9/L$  was 13 days (range 9-35 days). The median time to an Absolute platelet count of  $> 20 \times 10^9/L$  was 23 days (range 9-35 days), one patient had a graft failure who presented adequate recovery after infusion of cryopreserved bone marrow back-up. The median follow up time was 492 days (range 55 days-1127 days). 4 of the 16 recipients had relapsed. At the present time, 13 patients are alive. Relapse was the only cause of death and Transplant Related Mortality was zero.

**Conclusion:** We conclude that ASCT is a feasible and effective method of treatment for patients with high risk neuroblastoma. The inclusion of high-dose chemotherapy and autologous rescue have improved the chances of survival of children with high risk neuroblastoma in developing countries allowing to reproduce the results achieved in developed countries.

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**IMPACT OF NUTRITIONAL PARAMETERS ON OUTCOME AFTER PEDIATRIC HSCT**

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**Background:** Nutritional parameters represent modifiable factors to improve outcomes after HSCT. Pediatric studies linking weight to survival are over 10 years old, and analyses of prealbumin (PAB) levels have not examined the impact on survival.

**Methods:** We conducted a retrospective chart review of all pediatric HSCT at our institution from 7/1/2007 to 6/30/2011 (N = 77). Wilcoxon rank-sum test was used to compare weight characteristics as well as PAB and albumin levels (admission, days 0, +7, +14,+28, and +90 for albumin alone) between the autologous (auto) and allogeneic (allo) groups. Survival analyses utilized the Kaplan-Meier method and the log-rank test to compare differences. Effects on survival were examined with a Cox proportional hazards model and analyses of non-relapse mortality (NRM) incorporated competing risks.

**Results:** Mean weights as % of ideal body weight at admission were above 100% and not significantly different between the auto and allo groups (p = 0.80). BMI at admission was not significantly different between the auto and allo groups (19.5 and 19.3 respectively, p = 0.97). At day +30, the auto group had greater % weight loss than the allo group with mean weight loss of 1.7% (p = 0.01). In the auto group, weight loss at day +30 was associated with significantly worse day +100 and 1 yr survival compared to those who had weight gain (p = 0.03). The lowest median PAB level was 13.8 mg/dL on day 0 for all patients and 12.2 mg/dL on day +7 for auto patients. Similarly, the lowest median albumin level was 2.9 g/dL on day 0 for all patients and 2.8 g/dL on day +7 for auto patients. Differences between groups at these time points were statistically significant (p<0.05). Univariate analyses identified PAB levels below 15 mg/dL at day +7 as significantly decreasing day +100 and 1 yr survival in the allo group (p = 0.0003). Additionally, all patients with a PAB level below 12 mg/dL at any time between day 0 to +14 had worse day +100 and 1 yr survival (p = 0.023). Multivariate analysis of the combined groups demonstrated a significant impact of decreased PAB levels between day 0 to +14 on NRM, with a hazard ratio of 0.85 (95%CI 0.76-0.96, p = 0.006). Accordingly, this represents an increase in NRM risk of 120% per 5 mg/dL decrease in PAB.

**Conclusion:** Nutritional support should be maximized early in the transplant course. As PAB is decreased in the setting of inflammation, future studies should prospectively evaluate PAB in conjunction with inflammatory markers.

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**MOYAMOYA SYNDROME TREATED WITH ENCEPHALODUROARTERIOSY-  
NANGIOSIS FOLLOWED BY HEMATOPOIETIC CELL TRANSPLANTATION  
IN PATIENTS WITH SICKLE CELL DISEASE**

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**Background:** Patients with sickle cell disease (SCD) have a high risk of intracranial large vessel vasculopathy, leading to a proliferation of microvasculature at the base of the brain known as moyamoya syndrome. This confers a high risk of intraventricular hemorrhage and permanent neurologic deficits. Moyamoya syndrome can be treated surgically with a revascularization procedure called encephaloduroarteriosynangiosis (EDAS), which has been shown to decrease but not eliminate the risk of stroke. Hematopoietic cell transplantation (HCT) from a compatible sibling is the most effective way of preventing central nervous system (CNS) complications in SCD patients at risk for CNS events. There have been several reports of patients with SCD and moyamoya syndrome undergoing EDAS successfully; however, there have been no reports of these patients undergoing EDAS followed by HCT.

**Results:** We report six pediatric cases of patients with SCD who developed moyamoya syndrome, all of whom underwent EDAS followed by HCT. All patients underwent EDAS procedure successfully. One patient experienced a stroke less than a month after EDAS. Another patient developed a foot-drop post-EDAS, though imaging did not show any new areas of infarct. All patients underwent HLA-matched sibling-donor HCT. The chronic transfusion therapy was successfully discontinued in the two patients who had been on it prior to treatment. Post-transplant, one patient developed seizures, with imaging consistent with possible infarct; the patient was placed on antiepileptics and has not had subsequent seizures. In all follow-up imaging, there has been no progression of the patients' moyamoya syndrome.

**Conclusion:** These are the first reported cases of EDAS successfully followed by HCT in patients with SCD and moyamoya syndrome. Five of the six patients had no further CNS events, and all remained neurologically stable, with no progression of their moyamoya syndrome. HCT is the standard of care in patients with SCD at risk for CNS complications, leading to excellent stroke-free survival rates. Patients with moyamoya syndrome and SCD are at high risk of developing CNS complications. Transplant-eligible SCD patients who develop moyamoya syndrome may benefit from EDAS prior to HCT in order to minimize CNS complications. Further investigation by way of an international, multicenter prospective study is needed to determine the long-term outcome and potential benefits of this therapeutic combination.

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**COMPARISON OF SURVIVAL AND INCIDENCE OF GRAFT VERSUS HOST DISEASE IN FULLY MATCHED, SINGLE C MISMATCHED AND OTHER MISMATCHED UNRELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTS IN A PEDIATRIC POPULATION**

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It is well understood that undergoing hematopoietic stem cell transplant (HSCT) from an unrelated (URD) compared to a matched sibling donor (MSD) results in increased graft versus host disease (GVHD) and for the pediatric population this often but not always negatively impacts overall survival. In the current era of high resolution Class I / Class II typing there is a lack of clarity about the impact

**Table I. Supplemental Patient Data**

Patient	Presenting Symptoms of Initial CNS Event	Age at Diagnosis of Moyamoya Syndrome	Age at EDAS Procedure	Age at HCT	Post-HCT Complications
1	Seizures	11 years 6 months	12 years 2 months	12 years 8 months	Seizure, Possible Left Middle Cerebral Artery Infarct
2	Visual changes	13 years 2 months	Two-Step Procedure: 13 years 4 months and 13 years 7 months	13 years 9 months	None
3	Seizures	2 years 6 months	4 years 6 months	5 years 6 months	None
4	Left-Sided Hemiparesis	3 years	6 years 6 months	8 years 6 months	None
5	Seizures, Personality Changes	7 years 6 months	Two-Step Procedure: 8 years 10 months and 8 years 11 months	13 years	None
6	Eye pain	6 years	11 years 9 months	13 years 6 months	None