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

Chirnomas, D.[1], Lehmann, L.[2], London, W.[2], Duncan, C.[2], Powell, A.[4], Barry, E.[3] [1]Yale School of Medicine, New Haven, CT; [2]Dana-Farber Cancer Institute/Children's Hospital Boston, Boston, MA; [3]Sanofi Oncology, Cambridge, MA; [4]Children's Hospital Boston, Boston, MA

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 ≥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 ≥ 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 (± std error) was 4.97 ± 3.54 mg/g dwt liver at pre-SCT and 7.55 ± 4.37 mg/g dwt 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 dwt 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

Marsh, R.A.[1], Filipovich, A.H.[1], Allen, C.E.[2], McClain, K.L.[2], Weinstein, J.L.[3], Kanter Washko, J.[4], Skiles, J.[5], Lee, N.D.[5], Khan, S.P.[6], Lawrence, J.[1], Mo, J.Q.[7], Bleesing, J.J.[1], Jordan, M.B.[1,8] [1]Cincinnati Children's Hospital; [2]Baylor College of Medicine; Texas Children's Cancer Center; [3]Northwestern University Feinberg School of Medicine, Children's Memorial Hospital; [4]Tulane Medical Center; [5]Riley Hospital for Children; [6]Mayo Clinic; [7]Cincinnati Children's Hospital; [8]Cincinnati Children's Hospital

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

Chaparro, M., Estupinan, M. Fundacion HOMI Hospital de la Misericordia, Bogota, Colombia

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/m2 for 4 days), Etoposide (300 mg /m2 for 4 days), and Melphalan (60 mg/m2 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 x 10 9/L was 13 days (range 9-35 days). The median time to an Absolute platelet count of >20 x 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

Qudiemat, A.[1], Armeson, K.[2], Ragucci, D.[3], Nista, E.[4], Hudspeth, M.P.[1] [1]Medical University of South Carolina, Charleston, SC; [2]Medical University of South Carolina, Charleston, SC; [3]Medical University of South