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transplant, with chimerism from 80 to 100% donor cells. In conclusion, haploidentical HSCT with post-transplant cyclophosphamide is a feasible alternative for X-ALD lacking a suitable matched donor. Graft failure is still an obstacle that has to be better prevented.

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Busulfan, Melphalan, and Thiotepa Conditioning for Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) of Pediatric Patients with Acute Leukemia and Central Nervous System (CNS) Disease

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The standard of care for the transplantation of pediatric patients with acute leukemia and prior CNS disease is the use of total body irradiation (TBI), plus a CNS radiation therapy (RT) boost. However, the late effects of radiation can be prohibitive, especially in younger children or those who have previously received radiation therapy. We developed a chemotherapy-only cytoreductive regimen with the intent of targeting the CNS with agents that can readily cross the blood brain barrier and achieve high concentrations. We used the combination of Busulfan (1mg/kg every 6 hours x 3 days), melphalan (50mg/m^2/day x 2 days), and thiotepa IV (8.3mg/kg/day or 250mg/m^2/day x 2 days).

We treated six patients with acute myelogenous leukemia (AML (N=5) or acute lymphoblastic leukemia (ALL) with this regimen from July 1999 and February 2013. The median age at the time of HSCT was 2.8 years (range 1.7 to 13.4 years). Patients were in complete CNS remission (CR) CR1 (N=1), CR2 (N=3), CR3 (N=1), and CR8 (N=1). All six patients were treated with multiple intrathecal chemotherapy agents prior to transplant. Four of six patients received cranio-spinal radiation therapy (RT) prior to HSCT; RT was required to achieve a CNS CR in 3 of 4 of these patients. One patient received CNS RT post HSCT, while one patient was completely spared CNS RT.

Donors and grafts included unrelated mismatched umbilical double cord transplants (N=4) and matched related T-cell depleted bone marrow transplants (N=2). All six patients engrafted. One patient succumbed to infectious complications nearly 2 months post HSCT. The five other patients are still alive without marrow or CNS relapse at a median follow-up of 19.4 months post HSCT (range: 11.1 to 149.5 months) . While this represents a small patient series, this data provides evidence for a promising transplant chemotherapy-only regimen for the transplantation of pediatric patients with acute leukemia and CNS disease who are unable to receive TBI, and will be the focus of a larger prospective study.

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Acute Graft Versus Host Disease Following Sibling Donor Transplantation for Thalassemia Major

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Acute GVHD (aGVHD) remains a major challenge in allogeneic stem cell transplantation and is associated with significant morbidity. Though it is associated with a graft versus leukemia effect in SCT for malignant disorders, it has no benefit in SCT for non-malignant disorders such as thalassemia major.

This is a retrospective analysis of 321 patients who underwent allogeneic SCT for Thalassemia Major at our centre between Jan 1991 and Dec 2011. This included 205 males and 116 females with a median age of 7 years (range: 2 - 24). Patients who expired prior to 2 weeks or had primary graft rejection were excluded from this analysis. 6.9% of patients were in Lucarelli Class I, 36.4% in Class II, and 56.7% in Class III. Donors included matched sibling (n = 299) or other family donors (n = 22). Conditioning regimen was predominantly Busulfan based (n = 274) while 47 patients received treosulfan based conditioning. Graft source was mainly bone marrow (n = 286) while GVHD prophylaxis mainly was Cyclosporine with short course methotrexate (n = 301).

Acute GVHD (Grade I – IV) occurred in 125 patients (38.9%), grade II-IV in 28% and grade IV in 5.3%. Donor age ($p = 0.062$), type of conditioning regimen ($p = 0.07$), number of doses of methotrexate administered ($p = 0.05$), presence of veno-occlusive disease (VOD) [$p = 0.016$] and time to neutrophil engraftment ($p = 0.027$) were found to be significant risk factors for acute GVHD on a univariate analysis but only VOD ($p = 0.017$) and donor age ($p = 0.044$) remained significant on multivariate analysis. Resolution of GVHD was seen in 90.4% while 9.6% died either due to GVHD or infection. The 3 year overall survival was 80% ± 2.3% in patients with GVHD compared to 81.1% ± 2.9% in patients without GVHD ($p = 0.422$).

Acute GVHD is seen in 39% of patients undergoing SCT for thalassemia major but it does not have a significant impact on overall survival.

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Hemorrhagic Cystitis Following Hematopoietic Stem Cell Transplants in Children: Single Center Experience

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Background: Hemorrhagic cystitis (HC) is a fairly common and potentially severe complication observed after hematopoietic Stem cell transplantation (HSCT) which may result in morbidity and extended hospitalization. Its incidence in pediatric patients is unknown.

Methods: We performed a retrospective study on 900 pediatric patients who received HSCT after myeloablative or reduced intensity conditioning during 1992 – 2011 in our center. In all, sixty patients (43 male &17 female) developed HC: early in 35 patients and late in 25 patients. Median age of patients was 9.19years (range: 2-15). Major thaassemia (45%) and ALL (18.30%) were most common cause of transplantation. Patients received transplant from matched donor (n=45), 2 locus mismatched (n=8) and HLA-haploidentical (n=7). The source of stem cell were peripheral blood (n=40), bone marrow (n=15) and cord blood (n=5). Majority of patient (83.3%) received BU/CY conditioning regiment.

Results: The prevalence of HC was 6.7% in our patients who all of them had received allogenic HSCT. 4 patients had pervious history of HC. Acute graft versus host disease (GvHD) occurred in 46(76.7%) patients. There was no significant correlation between the grade of acute GvHD and

severity of HC (P-value>0.05). By quantitative PCR, a viral etiology for one or more viruses was found in 40 cases (CMV, HSV& BK). HC was managed with supportive care (blood and platelet transfusion, hydration and irrigation) in all patients. 4 of the patients required surgical interventions and cystectomy. 4 years Overall survival of patients was 56%. Main cause of death were sever HC (n=11) and disease relapse (n=9).

Conclusion: HC is caused by the interaction of several conditions such as donor type and preparative regimen intensity. This study shows that young age correlated with a lower incidence of severe HC. A prospective study is necessary to clarify the association between clinical factors such as age in the development of severe HC following HSCT in children.

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Radiologic Resolution of Malignant Infantile Osteopetrosis Skeletal Changes after Hematopoietic Stem Cell Transplantation

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Introduction: Hematopoietic stem cell transplantation (HSCT) is considered the only curative treatment of malignant infantile osteopetrosis(MIOP). This study evaluates the radiologic evolution of skeletal changes after HSCT in children with MIOP.

Methods: Twelve patients(8 male & 4 female, median age of 14.5 months) with proved MIOP underwent HSCT. Patients received transplant from relative matched donor(n=9), unrelated matched(n=1), unrelated mismatched cord blood(n=1) and HLA-haploidentical relative(n=1). The source of stem cell were bone marrow(n=7), peripheral blood(n=4) and cord blood(n=1). Baseline, 6th and 12th month post-HSCT whole body bone surveys were performed. All patients survived except one who died at 8 months due to infection.

Results: Baseline corticomedullary differentiation was not detectable in any patient, however by 6^{th} month it was perceivable in 3(p-value: 0.25) and by 12^{th} month in 9 patients(p-value: 0.004). Baseline endobone appearance was seen in long and flat bones of 11 and 12patients, respectively. Resolution of long bones endobone appearance was seen in 9patients by 6^{th} month(p-value: 0.008). None of 11patients had endobone appearance by 12^{th} month(p-value: 0.002), while flat bone endobone appearance was persistent in 10patients at 12^{th} month. By 6^{th} month, significant disappearance of rachitic changes in long bones was seen, however it was persistent in ribs in 11patients. By 12^{th} month, there was not any evidence of rickets in ribs and long bones of any patient(P-values<0.005). Of all subjects with baseline skull base sclerosis, by 6^{th} and 12^{th} month it was persistent in 9(p-value: 0.25) and 5patients(p-value: 0.03) respectively. The mean metaphysical band to femur length ratio was significantly higher at 6^{th} month compared to the baseline(7.56 ± 3.66 vs. 2.87 ± 1.25, p-value: 0.001)

Conclusion: This study demonstrated the resolution in skeletal changes of osteopetrosis after successful HSCT. Long bones rachitic changes and endobone impression were the first to resolve within 6 months after HSCT.

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Survival and Neurocognitive Outcomes Following Cranial or Craniospinal Irradiation Plus Total Body Irradiation Prior to Transplantation in Children with CNS Leukemia

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Purpose/Objective(s): Optimal management of pediatric acute lymphoblastic leukemia (ALL) patients with CNS involvement remains a challenge, with limited data to guide treatment. The goal of this study is to evaluate survival and neurocognitive outcomes among pediatric ALL patients with CNS involvement who underwent stem cell transplantation (SCT) and received cranial or craniospinal irradiation in addition to total body irradiation (TBI) as pre-transplant preparative regimen according to an institutional protocol.

Materials/Methods: A retrospective analysis was performed of pediatric ALL patients with CNS involvement who underwent SCT at our institution between 1986 and 2011. The Kaplan-Meier method was used to compute estimates of disease-free survival (DFS). Cox regression models were used to determine associations of patient and disease characteristics and treatment methods.

Results: Forty-one pediatric ALL patients underwent SCT with TBI as a preparative regimen and received additional cranial or craniospinal irradiation due to CNS involvement. Median age at diagnosis was 5 years (range 1 to 21 years). Twenty-six patients were standard-risk by NCI criteria, and 14 were high-risk. Five patients underwent transplant in first complete remission (CR), 25 in CR 2, and 11 in CR 3 or greater. All patients received a cranial boost; median cranial dose was 24 Gy (range 18-35.4 Gy). Eighteen patients received a spinal boost; median spinal dose for these patients was 18 Gy (range 15-24.6 Gy). Survival analysis from date of SCT revealed a 1 year DFS of 78%, 2 year 67%, and 5 year 67%. Univariate Cox regression revealed no statistically significant associations; however, omission of a spinal boost was associated with inferior DFS (HR 3.23, p=0.14). A combined CNS and bone marrow relapse prior to transplant was associated with an inferior DFS (HR 3.64, p=0.11), as compared with an isolated CNS relapse. 17/41 patients had an isolated CNS relapse, and analysis of these patients revealed a 1 year DFS of 88%, 2 year 81%, and 5 year 74%. A battery of neurocognitive testing was performed in 16 patients and at a mean of 4.4 years after transplant, mean post-transplant overall IQ was 103.7 (range 84-143). Pre and post-transplant neurocognitive testing in a subset revealed a mean overall IQ change of +4.8 points (range -1 to +9).

Conclusions: We show that addition of craniospinal irradiation to TBI is feasible in the preparative regimen for SCT in children with CNS leukemia and is associated with favorable DFS at 5 years post transplant, particularly in those patients with isolated CNS relapse. The use of craniospinal as opposed to cranial irradiation may be important in maximizing disease control. Post-transplant neurocognitive testing reveals average intelligence. Pre and post-transplant testing shows no change in IQ scores, though numbers remain small. CSI plus TBI is worthy of further protocol investigation.