Surgical management can be delayed by pancytopenia or other complications of PSCT. Transsphenoidal surgery has been shown to be more successful in improving vision if performed within 8 days of diagnosis. Emergent surgery is indicated for deteriorating vision, hemiparesis, or altered consciousness, while those with stable or resolving visual field deficits can be managed conservatively. Our patient was managed conservatively until engraftment. Transsphenoidal surgery was then performed, 9 days after diagnosis. At six months follow-up, his visual deficits had resolved but he continued to have diabetes insipidus.

GRAFT PROCESSING

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AUGMENTATION OF STANDARD UMBILICAL CORD BLOOD TRANSPLANTATION WITH ALDH^{br} CELLS: RESULTS OF A PHASE I STUDY IN PEDIATRIC PATIENTS

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Transplantation of unrelated donor umbilical cord blood (UCB) is limited by graft failure and engraftment delays. Strategies to facilitate engraftment are needed. Cord blood contains a population (0.5%) of cells expressing aldehyde dehydrogenase (ALDH^{br}), an intracellular enzyme highly enriched in hematopoietic stem and progenitor cells. The primary endogenous substrates for ALDH are retinaldehydes, oxidized to retinoic acid, which exert major effects on hematopoiesis. We hypothesized that augmentation of a standard UCB transplant with ALDH^{br} cells isolated from a portion of the graft would improve engraftment. Over the past 2 years, 21 pediatric patients with malignant (n = 7) and metabolic (n = 14) disorders prepared with myeloablative preparative regimens were transplanted with a UCB unit cryopreserved in a compartmentalized bag allowing for 80% of the unit to be administered as a conventional graft and 20% as purified ALDH^{br} cells, freshly isolated (n = 8) or primed with cytokines × 5 days (n = 13). Neither infusional toxicity nor an increase in unexpected adverse events were observed. The cumulative incidences (CI) of neutrophil (ANC 500 by day 42) and platelet engraftment (Platelets 50 k by day 180) were 92.9% (95% CI 73.1–100.0) and 73.1 (95%CI 41.7–100.0). These results were compared to a control group from the COBLT study, which contained similar patients (although it was not possible to match all characteristics between the 2 groups), where the CI of neutrophil and platelet engraftment were 77.9% (95% CI 67.9–87.9) and 64.9% (95% CI 51.6–78.2). These differences favored patients transplanted with ALDH^{br} cells at p = 0.01 and p = 0.02. Neutrophil engraftment occurred in a median of 19 versus 26 days in the ALDH versus COBLT patients. Platelet engraftment was accelerated to 58 days in the ALDH patients compared to 107 days in the COBLT patients. Significant accelerations in neutrophil and platelet engraftment were also observed in a subgroup analysis of metabolic patients alone. There were no differences seen between groups receiving freshly sorted versus primed ALDH^{br} cells. While preliminary, these results suggest that the infusion of ALDH^{br} cells facilitates overall engraftment, perhaps through a niche effect. Further investigation of mechanisms of action and a phase II study are underway.

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PHASE I TRIAL OF AUTOLOGOUS BONE MARROW MESENCHYMAL STEM CELL TRANSPLANTATION IN PATIENTS WITH DECOMPENSATED LIVER CIRRHOSIS

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Background: The standard treatment for decompensated liver cirrhosis is liver transplantation. However, it has several limitations. Recent animal studies suggest that bone marrow stem cell transplantation can lead to regression of liver fibrosis. The objective of this study was to determine the safety and feasibility of autologous bone marrow-mesenchymal stem cell transplantation in patients with decompensated liver cirrhosis. **Methods:** In this phase 1 trial, four patients with decompensated liver cirrhosis were included. Their bone marrow was aspirated, mesenchymal stem cells were cultured, and a mean 31.73 × 106 mesenchymal stem cells were infused through a peripheral vein. Primary outcomes were evaluating the safety and feasibility of the work. Secondary outcomes were evaluating changes in the model for end-stage liver disease score, and the quality of life of the patients. **Results:** There were no side-effects in the patients during follow-up. The model for end-stage liver disease scores of patients 1, and 4 improved by four and three points, respectively by the end of follow-up. Furthermore, the quality of life of all four patients improved by the end of follow-up. Using SF-36 questionnaire, the mean physical component scale increased from 31.44 to 65.19, and the mean mental component scale increased from 36.32 to 65.55. **Conclusion:** Mesenchymal stem cell transplantation seems to be feasible and safe in the treatment of decompensated liver cirrhosis.

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POST THAW COLONY FORMING UNITS (CFU) IS A STRONG INDEPENDENT PREDICTOR OF ENGRAFTMENT AFTER UNRELATED DONOR UMBILICAL CORD BLOOD TRANSPLANTATION (UCBT)

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Background: Unrelated donor umbilical cord blood has increased access to transplant for patients lacking matched donors. However, a non-engraftment rate of approximately 20% despite adequate total nucleated cell (TNC) dose remains a barrier to it's overall success. We hypothesized that certain properties of the UCB graft would be predictive of engraftment. **Methods:** We performed a retrospective analysis of 423 unrelated donor umbilical cord blood transplants (UCBT) performed at Duke between 2/11/2000 and 5/1/2007. Eligible units were required to have pre-cryopreservation (pre-cryo) data for TNC, CD34 +/- CFU. The units were obtained from 16 US public cord blood banks and were selected for transplantation by pre-cryo cell dose and HLA matching. Pre-cryo data was provided by the cord blood bank as part of routine banking practices. All units were thawed and washed in the Duke Stem Cell Laboratory before transplant. Post-thaw testing (TNC, viability, CD34, CFU) was performed by consistent personnel. Univariate and multivariate analyses were performed to identify significant pre-cryo, post-thaw, and baseline factors predictive of neutrophil and platelet engraftment. **Results:** Patients in the cohort were characterized as follows: 68% had malignancies, 61% males, 73% Caucasian and 38% CMV+. Graft/patient mismatching was present for HLA (93%), sex (50%) and race (24%). There was excellent correlation between pre-cryo and post-thaw TNC (r^2 = 0.92) and CD34 (r^2 = 0.68) content, but much weaker correlation for CFUs (r^2 = 0.27). In univariate analysis, pre-cryo/post-thaw CD34 (larger) and pre-cryo/post-thaw CFU (larger), pre-cryo/post-thaw TNC (larger), age (≤5 years), disease (non-malignant), weight (≤12 kg), CMV status (negative), recipient ethnicity (Caucasian), HLA match (5/6 or 6/6) were predictive of neutrophil and platelet engraftment. In the overall multivariate analysis of neutrophil engraftment, larger post-thaw CFU (<0.0001), larger post-thaw CD34 (p = 0.02), Male units (p = 0.01), 5/6 or 6/6 HLA match (p = 0.02) were significant. For platelet engraftment, larger post-thaw CFU (p = 0.002) and Caucasian recipients (p = 0.006) were predictive. **Conclusions:** Post-thaw CFUs are a strong independent laboratory predictor of neutrophil and platelet engraftment after UCBT. Efforts should be focused on developing a reproducible assay on CBU segments that would correlate with results obtained at thaw of the UCB unit and thus serve as a potency assay before UCB release from the bank.