Celiac Disease Transmitted By Unrelated Cord Blood Stem Cell Transplantation (CBST)
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Background: Celiac disease is due to intolerance to certain cereal proteins leading to immune-mediated small bowel villous atrophy and malabsorption. Specifically, the gliadin component of wheat, and the prolamin component of rye and barley are implicated in causing disease. BMT and CBST have been known to transmit immune-associated diseases such as diabetes mellitus immune thrombocytopenic purpura from an affected donor to transplant recipient.

Methods & Results: We observed the occurrence of Celiac disease in a patient a year following cord blood stem cell transplantation (CBST) for acute myelogenous leukemia (AML- FAB M2) in complete second remission (CR-2). The patient had no history of celiac disease prior to CBST nor any family member. The cord donor was HLA-identical unrelated male donor with HLA types: A3, B7 (w6), DR (B1), DR (B5). The family history of the donor was unavailable for celiac disease. The CBST was complicated by grade 2 skin Graft versus Host Disease (GVHD), which responded to steroid therapy. A year post transplantation she developed persistent mucous diarrhea with tinge of blood associated with abdominal cramps. Investigations for infectious causes such as CMV enteritis were negative and colonscopy did not reveal any evidence of GVHD. Gastrointestinal symptoms persisted and did not respond to steroid and prograf therapy. Subsequent duodenal and jejunal biopsy revealed subtotal villous atrophy with cryptic hyperplasia suggestive of celiac disease. Antigliadin IgA and IgG, reticulin IgA and Endomysial IgA antibodies were elevated. A diagnosis of post-CBST coeliac disease was made. She responded well to gluten-free diet and became symptom-free.

Discussion & Conclusion: A literature review identifies only from donor to recipient one previous example of transmission of celiac disease following HSCT. This case could be the second case of celiac disease following transplantation and the first one post CBST. An association of celiac disease with some HLA types, including DQA1.0501, and DQB1.0201, in conjunction with the haplotypes A30, B18, DR3, DRw52, and DQ2 was recently noted. The donor of this case exhibit haplotypes A30, B18, DR3, DRw52, and DQ2 alleles. The findings suggest transfer of celiac disease by cord stem cells and confirm the immune nature of the disease. In addition the propensity to develop T-cell non-Hodgkin lymphoma and transmission of celiac disease by CBST support T cell concept in celiac disease. Autoimmune enteropathy should be considered in patient with persistent diarrhea post hematopoietic stem cell transplant.

Non-Myeloablative (NMA) Allogeneic Hematopoietic Stem Cell Transplant for the Treatment of Patients with Hematologic Malignancies Using Busulfan, Fludarabine and Total Body Irradiation (BuFlu/TBI) Conditioning: Results of a Phase II Trial
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Introduction: Non-myeloablative (NMA) allogeneic transplant for the treatment of hematologic malignancies has become the standard of care for patients unable to tolerate myeloablative conditioning. The BuFluTBI transplant regimen was designed with the primary goal of reducing non-relapse mortality (NRM) while maximizing primary disease control in older and infirm patients.

Methods: Patients with high-risk hematologic malignancies were given an outpatient conditioning regimen of busulfan 3.2 mg/kg IV on day -5, fludarabine 30 mg/m2 IV on days -4, -3, -2, and 200 cGy of total body irradiation (TBI). Sources of hematopoietic stem cells were either from related or unrelated donors (at least 7/8 antigen match). GVHD prophylaxis was given with cyclosporine and mycophenolate mofetil. Clinical predictors of response were evaluated utilizing Cox Proportional Hazards Model.

Results: 147 patients were enrolled from 2005-2011. 86 (59%) with myeloid disease and 61 (41%) with lymphoid disease. The median age was 64, and the median comorbidity index (HCT-CI) score was 3. The overall survival (OS), with 2 years median follow-up, was 60% at 1 year and 48% at 2 years, with projected OS 37% at 5 years. Relapse rates were 29% at 1 year and 33% at 2 years, with relapse mortality of 13% at 1 year, and 20% at 2 years. NRM at 1 year was 27% and 33% at 2 years. 54% of patients developed early or late grade II-IV acute GVHD (aGVHD), and 67% of patients developed cGVHD within 2 years. On multivariate analysis, amongst 92 evaluable patients, HCT-CI score greater than 4, pre-transplant KPS <90, delayed platelet engraftment >15 days, and aGVHD >4.31 (1.80-10.33) 0.001, + cGVHD 2.77 (1.44-5.32) 0.002, were found to be independent predictors of poor survival as demonstrated in the table.

Conclusions: In an infirm elderly population with a high HCT-CI, BuFluTBI is an effective regimen with favorable OS with acceptable levels of NRM.