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SEVERE TRANSPLANT ASSOCIATED MICROANGIOPATHY (TAM) MAY BE LINKED TO SEVERE ORGAN INJURY IN PEDIATRIC PATIENTS TREATED WITH SIROLIMUS (SIR) AND CALCINEURIN INHIBITOR (CNI) FOR PREVENTION OR TREATMENT OF GRAFT-VS-HOST DISEASE (GVHD)

Rosenthal, J., Bolotin, E., Pawlowska, A., Oliver, C., Forman, S. City of Hope, Duarte, CA

The addition of SIR to CNIs for treatment of GVHD may result in a higher than expected incidence of TAM. We reviewed the impact of organ injury or active GVHD on the clinical manifestation of TAM in 2 groups of pediatric patients (pts): 1) pts received SIR and tacrolimus (TAC) for prevention (GP); 2) pts treated for active GVHD (TP).

Methods: A retrospective chart review of all pediatric pts who received SIR/CNI for prevention or treatment of GVHD. TAM was defined according to the International Working Group for TAM. The risk periods were defined as days –1 to +60 in PG and day+1 to day +30 after the last dose in TG.

Results: Forty-five pts were identified. The median age was 9.1 yr (2.9–22) and 14.7 yr (2.9–22) in the PG (n = 21) and TG (n = 24), respectively. Preparative regimens were TBI-based in 64%. Diagnoses included ALL (40%), AML (27 %), NHL (9%), Fanconi's (4 %), other (9%). SIR and TAC levels were monitored in all pts, and doses were targeted to maintain levels within the desired range (WDR) of 2–10 ng/ml for both. The median follow up is 31 months. TAM criteria were met in 5 PG pts (23.8%) and 10 TG pts (41.6%). Two PG patients died from non-TAM related causes (VOD, n = 1 and infection, n = 1). TAM presented in both patients as hemolytic uremic syndrome. One patient had seizures secondary to thrombotic thrombocytopenic purpura (TTP). TAC and SIR levels in this pt. were WDR. In the remaining 12 PG pts TAM findings were asymptomatic. SIR/TAC levels in these patients were all WDR. Among 10 TG pts that met TAM criteria, 2 pts had HUS and one severe TTP. All 3 patients with complicated TAM died (HUS, n = 1, other causes, n = 2). Two of TG pts with laboratory, but not clinically apparent TAM died (fungal infection, n = 1, IP n = 1). In all TG pts with TAM either TAC (n = 7) or SIR (n = 6) levels exceeded WDR. The following possible variables were analyzed: age, conditioning regimen, diagnosis, HLA disparity. In the PG, only organ failure or GVHD could be identified as risk factors. In the TG, TAC or SIR levels exceeding WDR and organ injury from acute or chronic GVHD were associated with an increased risk for clinically significant TAM.

Conclusion: Laboratory TAM occurs in about 30% of pts treated with SIR/CNI; however, clinically significant TAM occurs only in a minority of pts. Severe TAM may be associated with organ injury from GVHD or other reasons. Monitoring TAC or SIR levels may prove to be critical in patients with progressive organ injury or GVHD.

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OUTCOMES OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN RELAPSED GOOD RISK ACUTE MYELOCYTIC LEUKEMIA (AML) CARRYING T(8:21) OR INV(16)

Kim, B.-S.[1], Lim, J.H.[2], Yi, H.G.[2], Bang, S.-M.[3], Kim, I.[4], Lee, D.[5], Yoon, S.-S.[4], Park, S.[4], Kim, B.K.[4] [1] Seoul National University Boramae Hospital, Seoul, Korea; [2] Inha University Hospital, Incheon, Korea; [3] Seoul National University Bundang Hospital, Seongnam, Korea; [4] Seoul National University Hospital, Seoul, Korea; [5] Seoul National University Hospital, Seoul, Korea

Objectives: Patients with acute myelocytic leukemia (AML) with favorable cytogenetics such as t(8;21) and inv(16) are classified as good risk group and are not subject to hematopoietic stem cell transplantation (HSCT) frontline. However there are limited data following HSCT in relapsed good risk AML. Since allogeneic HSCT has been regarded traditionally as the only curative option in this population, we evaluated the outcomes of the patients who were treated with allogeneic HSCT in relapsed good risk AML carrying inv(16) or t(8:21).

Methods: We evaluated the outcomes of 22 consecutive patients who underwent allogeneic HSCT with either myeloablative (n = 17) or reduced-intensity conditioning (RIC) regimen (n = 5) between January 1997 and May 2007 at Seoul National University Hospital.

Results: Among 22 patients (median age 33, 18–70), 13 patients were classified as AML with t(8;21), 9 patients as AML with inv(16). 13 patients received sibling donor transplantation and the remaining 9 patients received unrelated donor transplantation. Median follow up duration was 8.3 months (range: 5.9 – 10.7 months). 20 patients attained remission after HSCT and 10 patients relapsed after remission with HSCT, 8 (61.5%) with t(8;21) and 2 (22.2%) with inv(16). At the time of analysis, only 7 patients are alive (3 patients (23%) with t(8;21), 4 patients (44%) with inv(16). 2 patients with inv(16) were lost to follow up. 13 patients (61.5%) expired, 10 with t(8;21) and 3 with inv(16). 9 patients with myeloablative conditioning regimen and 4 patients with RIC regimen expired. There was no statistical difference between the myeloablative and RIC regimen groups (p = .14). The main causes of death were relapse (53.8%, 7 patients), infection (23%, 3 patients) and GVHD (23%, 3 patients). 3-year survival rate was 43.8%. However, in patients with t(8;21) AML (n = 13), 3-year survival rate was 28.7%. On the contrary, in patients with inv(16) AML (n = 9), 3-year survival rate was 65.8%.

Conclusion: Patients with relapsed favorable risk AML showed divergent outcomes after allogeneic HSCT according to cytogenetic abnormalities. Patients with relapsed t(8;21) AML particularly exhibited high relapse rate and poor prognosis after allogeneic HSCT which is similar to treatment outcome of poor risk group AML. New treatment approaches including frontline HSCT with either allogeneic or autologous approaches should be tried in a prospective setting in this population.

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ROLE OF ANTI THYMOCYTE GLOBULIN (ATG) PRIOR TO UNRELATED DONOR STEM CELL TRANSPLANTATION (URD SCT) IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES: A SINGLE CENTER EXPERIENCE

Ganguly, S., Koya, B., Divine, C., Abhyankar, S., Aljitawi, O., Deauna-Limayo, D., Bodensteiner, D.C., Skikne, B.S., McGuirk, J.L. University of Kansas Medical Center, Kansas City, KS

Introduction: Long-term outcome in patients undergoing URD SCT depends partly upon the balance between complications from graft versus host disease (GVHD) and graft versus leukemia (GVL) effect. Use of ATG prior to URD SCT in an attempt to decrease the incidence and severity of GVHD may actually increase the risk of relapse secondary to reduced GVL effect.

Methods: In an attempt to examine whether addition of ATG provides long-term disease control in patients with hematologic malignancies undergoing URD SCT, we retrospectively evaluated our experience and analyzed the outcomes of URD SCT with or without ATG in patients with hematologic malignancies from 1995 to 2007. Fisher's exact test with two-tailed comparison was used for statistical purposes.

Results: Forty-six males and 22 females (n = 68) of median age 47 years (range: 15–64 years) were treated. Most common indication of transplantation was AML (n = 28) followed by CML (n = 12) and NHL (n = 12). Twenty-eight patients received ATG based regimen. Sixty-two of 68 patients engrafted (91%). Median time for neutrophil recovery was 15 days. There was no difference in the engraftment kinetics between ATG and non-ATG group of patients. Seventeen (25%) patients died within 100 days of transplantation. Median duration of follow-up was 12.6 months (range: 7–1026 days). Overall, 37 patients (53%) of this cohort died after transplantation. Of all the patients that died, 11 (39%) received ATG and 26 patients (65%) did not receive ATG ($p<0.05$). Infection was the commonest cause of mortality (n = 15; Five in the ATG group and 10 in non-ATG group; p = 0.5). Graft versus host disease was the direct cause of death in 6 patients (3 of them had received ATG) and 6 patients died from relapse of their disease (3 patients received ATG). These differences were not statistically significant (p = 0.6). Overall survival (OS) of all patients was 50% at 1 year and 47% at 4 years. There was no difference in the OS at 1-year between the ATG (64%) and non-ATG groups (40%) (p = 0.08), whereas at 4 years, OS in the ATG (60%) was superior to the non-ATG group (35%) ($p<0.05$).

Conclusion: Patients who received ATG as a part of the preparative regimen prior to URD SCT seemed to have a better long-term survival compared to patients that did not receive ATG. Use of ATG did not have any impact on relapse, infection rate or GVHD related mortality.