Title	Intensive chemotherapy with peripheral blood stem cell (PBSC) support in the treatment of leukemia relapse after allogeneic bone marrow transplantation: clinical results and chimerism findings
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S-HM-1

Fludarabine, Mitoxantrone and Dexamethasone (FND) in the Treatment of Indolent Lymphoid Malignancies

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Background: Indolent lymphomas are in Chinese. We evaluated prospectively the combination of fludarabine, mitoxantrone and dexamethasone (FND) in the treatment of indolent lymphomas in this population.

Patients and Methods: There were 44 men and 20 women, with a median age of 61 (33 -72) years. The diagnosis included follicular lymphoma (FL) (n=28), chronic B cell leukemia (B-LPD) (n=16), mantle cell lymphoma (MCL)(n=4), marginal zone B cell lymphoma (MZBL) (n=4), Maltoma with diffuse component (n=8), and T cell lymphoma (n=4). A total of 28 cases (43%) were treated at diagnosis (Dx) while 36 cases (57%) at relapse. The FND regimen comprised fludarabine (25mg/m^2/day x3), mitoxantrone (10mg/m^2x1) and dexamethasone (20mg/day x5), given at monthly intervals for six courses as outpatient, with pneumocystis prophylaxis.

Results: Sixty cases were evaluable. The overall response rate was 70% with complete response (CR) and partial response (PR) rates of 57% and 13% respectively. 17 patients achieving CR were further consolidated with rituximab for minimal residual disease eradication. Therapy was not completed in 15 cases (23%) because of infection (n=8) or rapid disease progression (n=7). A high CR rate was observed in grade 1/ 2 FL at Dx (10/10, 100%), T cell lymphoma (3/4, 75%), MZBL (3/4, 75%) and Maltoma (4/6, 66%). Intermediate response rates (CR+PR) were seen in grade 1/ 2 FL at relapse (6/9, 66%) and B-LPD (5/11, 56%). The response rates in patients previously treated with purine analogues and anthracycline were 60% and 55% respectively. Diseases with low response rates included grade 3 FL (1/ 3, 33%), MCL (1/4, 25%) and transformed B-LPD (0/3, 0%) Prolonged marrow suppression and septicemia (n=12) occurred in elderly (age>65, n=5) and heavily pretreated cases (>6 courses, n=6). Opportunistic infections included tuberculosis (n=4), cytomegalovirus gastritis (n=1) and cryptococcosis (n=1). Hepatitis B carriers (n=7) on prophylactic lamivudine did not suffered reactivation. At a median follow up of 13.8 months, disease progression was observed in 6 cases (5PR, 1CR). Sixteen patients have died, 13 due to disease, 1 each from sepsis, cirrhosis and lung cancer.

Conclusions: FND appears to be a safe and effective treatment in a wide spectrum of indolent lymphoproliferative disease in Chinese, especially with T-lineage disorder. Prudent prophylaxis for opportunistic infections is required.

S-HM-2

Intensive Chemotherapy with Peripheral Blood Stem Cell (PBSC) Support in the Treatment of Leukemia Relapse after Allogeneic Bone Marrow Transplantation: Clinical Results and Chimerism Findings

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Background: Disease relapse is the commonest cause of treatment failure after allogeneic bone marrow transplantation (BMT). We treated 20 consecutive leukemia relapses with intensive chemotherapy and peripheral blood stem cell (PBSC) to minimize neutropenia and maximize synergism of chemotherapy and GVL effect.
Material and Methods: The patients included 10 men and 10 women (median age = 31,range 17-49). The diagnosis was acute myeloid leukemia (AML) (n=8), acute lymphoblastic leukemia (ALL) (n= 6), chronic myeloid leukemia (CML) in blastic transformation (BT)(n= 6). The median time to relapse of 13 months (range 2-92), with extramedullary disease (EMD) in 8 cases. Chemotherapy was idarubicin 6mg/m^2× 5, cytosine arabinoside 600mg/m^2× 5, etoposide 150mg/m^2 × 3 (ICE). Three patients underwent a second course of chemotherapy with PBSC. A series of polymerase chain reaction (PCR) based microsatellite markers was used to quantify the ratio of donor and patient DNA. Minimal residual disease (MRD) PCR assessment was done in 5/13 responding cases.
Results: The PBSC harvest yielded a median of 6.3× 10^8/kg lymphocytes (range 2.9-11.9) and 2.3× 10^6/kg CD34+ve cells (range 0.9-5.2). There were two treatment-related deaths (10%). The median times for neutrophil and platelet recovery were 12 (range 9-18) and 14 days (range 10-18). Five patients (2 AML/ 3 CML-BT) did not respond, and 13 cases (65%) achieved complete remission (CR). Three patients died in remission due to GVHD. Four patients, without significant GVHD, relapsed with EMD in the breast, testis, retroperitoneum and pelvis at 2 to 10 months. The median follow up of the 7 surviving cases was 7 months (range 3-19). Donor DNA in the marrow at relapse ranged from 0% to 100%. All cases with complete donor chimerism responded, while patients with complete lost of graft remained refractory. In 11 case of mixed chimerism (2-86% donor DNA), 8 cases (73%) achieved CR. Complete donor chimerism was demonstrated in 8 cases in persistent CR. MRD assessment in 5 cases showed no MRD in 4 cases. One case remained MRD positive at CR, but fatal GVHD precluded donor lymphocyte infusion (DLI). Two patients reverted to MRD positivity and one relapsed before DLI was given.
Conclusion: ICE and PBSC is an effective salvage for acute leukemia relapse after BMT, especially before donor chimerism is lost. Monitoring of MRD, use of DLI, and improved GVHD control may improve clinical results.