S-HM-5

Methylation of p15 and p16 genes in Adult Acute Leukemia : Lack of Prognostic Significance

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Background: Gene promoter methylation is an epigenetic mechanism of transcription inactivation. In this study, we investigated the frequency and prognostic significance of p15 and p16 gene methylation in adult acute leukemia.

Method: The methylation specific polymerase chain reaction (MS-PCR) was used to analyze p15 and p16 gene methylation in 49 cases of acute lymphoblastic leukemia (ALL) and 29 cases of acute myelogenous leukemia (AML).

Results: At presentation, 93 % of cases in AML (8/8 M1, 10/11 M2, 2/2 M4, 5/6 M5 and 2/2 M6) showed p15 methylation, but none showed p16 methylation. In ALL, 57% (5/8 T-ALL, 14/26 common-ALL, 4/5 pre-B ALL, 1/3 early B precursor ALL and 4/7 mixed lineage ALL) showed p15 methylation. Only 6% showed p16 methylation, all of whom had concomitant p15 methylation. One patient acquired p16 methylation during relapse. For 23 ALL cases karyotyped, p15 methylation was found in 6/9 cases with normal karyotype, 3/7 cases with the Philadelphia chromosome, 3/3 cases with 9p-, 2/2 cases with complex karyotypes and 1/1 case with hyperdiploidy. Three more cases with unsuccessful karyotyping but BCR/ABL fusion showed p15 methylation as well. Five ALL patients were tested serially for minimal residual disease (MRD) with MS-PCR that has a sensitivity of 10^{-4} to 10^{-5}. All showed continuous positive MS-PCR that heralded hematologic relapse. The prognostic significance of p15 methylation was tested in ALL patients, showing no impact on complete remission, 5-year overall survival and 5-year disease free survival.

Conclusion: p15 but not p16 gene methylation is frequent in adult acute leukemias. p15 methylation at diagnosis was of no prognostic significance in ALL, but might be useful for monitoring MRD.

S-HM-6

Unmanipulated Bone Marrow Transplantation from One-Hla Antigen Mismatched Siblings Carries High Transplant-Related Mortality Compared with the Hla-Identical Counterparts

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Introduction: Allogeneic BMT is considered the curative treatment for many hematological malignancies but is often limited by the lack of donors. The use of sibling donors who are one-HLA antigen mismatched may increase the availability of transplants but its effects on survival and transplant-related mortality remained undefined. We compared the treatment outcomes of BMT from HLA-identical siblings (MS), one HLA-antigen mismatched siblings (MMS) and matched unrelated donors (MUD).

Patients and Methods: Medical records of patients who have received allogeneic BMT in Queen Mary Hospital from March 1990 to Februrary 2000 were reviewed. HLA of patients and donors were defined by DNA techniques. All patients received standard anti-microbial therapies and prophylaxis against GVHD.

Results: 294 patients received BMT from MS (CML=102, AML=106, ALL=38, Others=48). 20 patients from MMS (CML=13, AML=3, ALL=1, Others=3) and 44 patients from MUD (CML=22, AML=16, ALL=3, Others=3). They had no significant difference in terms of age at presentation, neutrophil (ANC $> 0.5 \times 10^9$/L) and platelet engraftments (platelet count $>25 \times 10^9$/L without transfusion). The median survival of patients receiving BMT from MS was 110 months whereas those from MMS and MUD were 13 and 10 months respectively ($p<0.005$). To eliminate the effects related to the difference in disease diagnoses and status at transplantation, subgroup analysis on patients with CML-CP was performed. 83 patients had received BMT from MS, 9 from MMS and 14 from MUD. BMT recipients from MUD had a significantly younger age at BMT, longer duration of disease prior to BMT and slower platelet engraftment when compared to the MS counterpart ($p<0.05$). At 100 months post BMT, the overall survival of BMT recipients from MS was 80%. The median survival of patients receiving BMT from MMS and MUD was 15 and 30 months respectively. ($p<0.001$ compared to MS). Of the 9 patients in the MMS group, 4 died of acute GVHD (Grade IV) early post BMT (1.5 ± 0.45 months) and 1 died of disease relapse at 15.1 months.

Conclusion: The results showed that BMT from MMS and MUD carried high transplant-related mortality compared with that from MS. Modification of post-transplant immunosuppression and/or donor T-cells depletion might alleviate the severity of GVHD in that situation.