S-H-3

A COMPARISON OF TBI AND NON-TBI CONDITIONING REGIMENS IN PATIENTS UNDERGOING MATCHED-UNRELATED BONE MARROW TRANSPLANTATION AKW Lie, AYH Leung and RHS Liang. Division of Haematology and Oncology. Department of Medicine. The University of Hong Kong

Allogeneic bone marrow transplantation (Allo-BMT) has been widely used for the treatment of haematological malignancies. In patients without HLA-matched siblings, BMT from matched-unrelated donors (MUD) becomes an alternative choice. Total body irradiation (TBI) is used conventionally in MUD BMT conditioning but it is associated with severe side effects. In allo-BMT conditioning, busulfan-cyclophosphamide (Bu-Cy) was shown to be as effective as Cy-TBI. In MUD BMT, however, there has been concern that the use of Bu-Cy may increase the risk of graft rejection. The present study investigated the effects of Bu-Cy conditioning on the outcome of patients undergoing MUD BMT. Since December 1998, 8 patients (CML=5; AML=3) underwent MUD BMT using busulfan (16 mg/kg) and cyclophosphamide (150 mg/kg) as conditioning. (Mean age 32.8± 3.3). As historical control, the outcomes of 28 patients (CML=16; AML=7; Biphenotypic acute leukaemia=2; ALL=2; MDS=1) who underwent MUD BMT using TBI containing regimen [Bu (7 mg/kg)-Cy (50mg/kg)-TBI (12Gy) = 18; Cy (120mg/kg)-TBI (12Gy) = 10] since 1992 (Mean age 29.3± 1.7) were also analyzed All patients received standard GVHD and anti-microbial prophylaxis. The average no. of days requiring TPN (as a result of oral mucositis) was significantly lower in the Bu-Cy group (18±3.6 days) compared with the control (31.9±4.1 days, Mann-Whitney U Test $p<0.05$). There were no differences in neutrophil (ANC > 0.5 x 10^9/L) and platelet (>25 x 10^9/L without transfusion) engraftments between the 2 groups. The Bu-Cy group had less veno-occlusive disease (VOD) (2/8 vs 11/28 in control) but more haemorrhagic cystitis (HC) (3/8 vs 5/28 in control) though the differences were not significant (Chi-Sq Test $p>0.05$). Patients in the Bu-Cy group also had a significantly lower occurrence (1/8) of severe GVHD (Overall grade >=2) than the control group (18/28) (Chi-Sq Test $p<0.05$). Transplant-related mortality (TRM) within 100 days after BMT was 0 in the Bu-Cy group but was 7 (out of 28) in the control (GVHD related = 4; Regimen-related toxicity = 2; Graft failure = 1). The difference, however, did not reach statistical significance (Chi-Sq Test $p>0.05$). There was no difference in the occurrence of early graft failure in both groups of patients (1/8 in the Bu-Cy group vs 3/28 in the control). In conclusion, we have shown that the use of Bu-Cy during conditioning in MUD BMT had no adverse effect on neutrophil and platelet engraftments and did not increase the occurrence of graft failure. On the other hand, the use of TBI-containing regimen in marrow conditioning was associated with increased severity of oral mucositis and increased risk of VOD and severe GVHD and a higher transplant-related mortality.

S-H-4

A STUDY OF THE ROLE OF POLYOMA VIRUS IN HAEMORRHAGIC CYSTITIS IN BONE MARROW TRANSPLANTATION PATIENTS Leung AYH[1], Lie AKW[1], Liang RHS[1], Yuen KY[2], C Suen[1] and Kwong YL[1] Division of Haematology Department of Medicine[1] and Department of Microbiology[2] The University of Hong Kong

Haemorrhagic cystitis (HC) is a common occurrence in bone marrow transplantation (BMT) recipients. In Queen Mary Hospital (QMH), its prevalence was 13.6%. While early onset HC is related to the toxicity of cyclophosphamide included in the conditioning regimen, the causes of late onset HC remain undefined. Polyomavirus, in particular, BK virus (BKV) has been detected by non-quantitative methods in the urine of patients with HC, and have been incriminated as the causative agents. We hypothesize that the severity of viruria is an accurate predictor of the development of HC and is directly related to the degree of immunosuppression. In this study, consecutive patients undergoing BMT in QMH were recruited. 24 hour urine for amplification of viral DNA by polymerase chain reaction (PCR), spot urine sample for analysis of cytopathic changes in uroepithelial cells and electron microscopy (EM) for viral inclusions were performed weekly. Simultaneously 10 ml of citrated blood was taken for viral DNA analysis by PCR. Urine dipstix is performed everyday for each patient throughout the BMT period. Target sequences from the DNA extracted from the urine and blood were amplified by PCR. To confirm specific amplification, PCR products from selected cases were sequenced. Specimen containing viral target sequence was subject to quantitative PCR (PE Applied Biosystem) to measure the number of viral DNA copies. In the 9 patients tested, 4 of them had HC (2 matched-unrelated and 2 allogeneic BMT). PCR for BK DNA were positive in all 4 patients whereas EM and cytology were positive in 3 and 1 patient respectively. In the 5 patients without HC (3 autologous and 2 allogeneic BMT), PCR for BK DNA and cytology were positive in 3 and 1 of them respectively. None of them was EM positive. Amplification of BK DNA in free urine and its sediment resulted in a distinct 95 bp band and the PCR product was confirmed by automated sequencing. Prospective quantification of BK viruria in a typical patient showed that excretion of BK virus increased from D7 and reached a peak on D14 corresponding to the period of neutropenia. Significant viral excretion persisted until D35 when the patient was discharged from the hospital. BK virus in urine was also detected by EM and cytology on D14 and D21, corresponding to the time of peak viral excretion measured by Q-PCR. The latter was followed by the occurrence of haemorrhagic cystitis which occurred from D24 to D34. In summary, BMT recipients have a high prevalence of BK viruria. Non-quantitative PCR for BK DNA in urine, although being sensitive, was non-specific as asymptomatic patients also excreted BK virus in urine. With the use of quantitative PCR, it was found that BK virus excretion in urine increased during period of neutropenia and the peak rise in excretion preceded the occurrence of clinical haemorrhagic cystitis. The establishment of a causative and temporal relationship will improve surveillance and will facilitate further study into the pathogenesis of haemorrhagic cystitis and its treatment.