CYTOKINE RELEASE SYNDROME IN HAPLOIDENTICAL PERIPHERAL HEMATOPOIETIC STEM CELL TRANSPLANT. AN UNDERESTIMATED RISK FOR TRANSPLANT-RELATED MORTALITY?

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Background: Haploidentical haematopoietic stem cell transplant (haplo-HSCT)with post-transplant cyclophosphamide (with both PBSC and BM) has been associated with cytokine release syndrome(CRS) between day 0 and day 4.
Herein, we describe the clinical features of CRS within our haplo-HSCT population with malignant conditions.
Patients and Methods: between August2010 and December2022, 70 patients underwent haplo-HSCT at King's College Hospital; the outcome of 46 patients with a malignant disease (and negative blood culture between day 0 and day 4) are reported. Haplo-HSCT was performed with G-CSF mobilized PBSC. GVHD prophylaxis consisted of PTCY 50 mg/kg(d+3 and +4),mycophenolate and tacrolimus as previously described.
Results: One-year and three-year OS for CRS grade 0-1, 2, 3 were: 73% and 49%, 69% and 59%, 25% and 0%, respectively (p-value 0.01). Median OS for CRS grade 1, 2, 3 was 40, 53 and 4 months, respectively. Global TRM for CRS grade 1, 2 and 3 was 30%, 35% and 100%(p-value 0.0001).Multivariate analysis for TRM adjusted for CRS grade, CD34+ dose and age at transplant, disease status at time of transplant, and performance status showed that high CRS grade is associated with increased TRM(Hazard ratio 6.684, p-value=0.0093, 95% confidence interval 1.367 to 26.76). Relapse rate was evaluable only in CRS grade 0 to 2 because all CRS grade 3 patients succumbed to TRM. There was a lower trend of relapse in CRS grade 2 with a cumulative incidence of relapse of 25% compared to 31% in CRS grade 0-1 patients (p-value 0.06).
Conclusions: CRS grade3 seems to be a rare complication in our study, it is associated with a very high rate of TRM. Although patient with CRS grade 2 have a better survival and reduced relapse rate, it is unclear if strategies are needed to mitigate lethal effect of CRS grade 3 and if these action will not increase the risk of relapse or graft failure.