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IMPACT OF DONOR-SPECIFIC ANTI-HLA ANTIBODIES ON ENGRAFTMENT FAILURE AFTER UNRELATED DONOR HEMATOPOIETIC CELL TRANSPLANTATION

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Graft failure (GF) is one of the major concerns after allogeneic hematopoietic cell transplantation (HCT), and still remains an important cause of morbidity and mortality. Although earlier reports have associated the presence of donor-specific anti-HLA antibodies (DSAs) with increased risk of GF after unrelated (URD) HCT, recent studies have failed to confirm this association. Therefore, to validate DSAs as a predictor of GF in URD setting, we retrospectively evaluated the impact of DSAs on engraftment failure in 303 consecutive patients who underwent URD-HCT from January 2008 to December 2017 at our institution. DSA evaluation was performed with Single Antigen Beads (SAB) panels. The probabilities of neutrophil engraftment (NE), platelet engraftment (PE), and GF were assessed on the basis of the cumulative incidence function and compared among groups with Gray's test. Death or relapse before engraftment or GF were competing events. Fine-Gray competing risk regression models were used to identify the risk factors in the multivariate analysis. The prognostic effect of GF on overall survival was assessed through a Cox regression model, using GF as a time-dependent variable. All statistical analyses were performed with EZR. Overall, eleven patients (3.63%) were DSA-positive, with a median DSA strength of 4681 MFI (range, 1144 to 22039) at URD-HCT. The cumulative incidence of NE at day +28 was 87.1%, with a median engraftment time of 21 days (range, 10 to 42). The cumulative incidence of PE at day +28 was 68%, with a median engraftment time of 24 days (range, 10 to 159). In univariate regression, the presence of DSAs was associated with inferior NE (SHR 0.59; 95%CI: 0.36-0.98; P=0.042). DSAs also adversely influenced PE (SHR 0.61; 95%CI: 0.43-0.87; P=0.007). Multivariate competing risk analysis showed that the presence of DSAs was significantly associated with NE (SHR 0.51; 95%CI: 0.28-0.90; P=0.021) and PE (SHR 0.62; 95%CI: 0.40-0.96; P=0.036). The cumulative incidence of GF for the entire cohort was 10.6% (95%CI:7.4-14.3%). The cumulative incidence of GF in patients with DSAs (36.4%; 95%CI: 10.2-63.9) was significantly higher than that in patients without DSAs (9.6%; 95%CI: 6.6-13.3) (P=0.004). Among the 11 DSA-positive patients, the median DSA strength for patients with GF was 10813 MFI (range, 4681 to 22039) versus 2993 MFI (range, 1144 to 15348) for those who engrafted (P=0.014). In univariate competing risk regression, the presence of DSAs was highly predictive for the occurrence of GF (SHR 4.18; 95%CI: 1.60-10.9; P=0.003). Multivariate analysis demonstrated that the presence of DSAs was independently associated with GF (SHR 5.76; 95%CI: 1.88-17.6; P=0.002). GF as a time-dependent variable was significantly associated with inferior overall survival (HR 6.87; 95%CI: 4.42-10.68; P<0.001). In conclusion, our results corroborate previous studies and validate the presence of DSAs as an important risk factor for engraftment failure after URD-HCT.

Key words: DSAs, graft failure, unrelated donor.