Hemorrhagic Cystitis caused by the BK virus decreases Survival Post-Allogeneic Stem Cell Transplantation

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Introduction: BK virus (BKV) reactivation usually occurs during the immunosuppressive therapy following allogeneic Stem Cell Transplantation (allo-HSCT) and the most common presentation is hemorrhagic cystitis (HC-BKV) Studies have shown that HC-BKV is a serious cause of morbidity after allo-HSCT and is associated with prolonged hospitalization, but little is known about the real impact on overall survival (OS).
Objectives: To evaluate the impact of HC-BKV in OS, factors associated with OS, and risk factors for HC-BKV following allo-HSCT.
Methods: We retrospectively reviewed the medical charts of 221 patients who underwent allo-HSCT at Hospital Israelita Albert Einstein from July 2007 until Dezember 2014. HC-BKV was defined by the presence of any degree of unexplained hematuria and positivity for BKV in a urine sample by quantitative polymerase chain reaction (PCR) assay. Risk of relapse risk was estimated using the same criteria used by Sorror. Overall survival (OS) was estimated by the Kaplan-Meier method. Gray model was used for regression analysis of factors associated with the development of HC. Hazard ratios (HRs) were estimated by a Cox multivariable proportional hazards model, considering HC,
Results: From the sample of 221 patients, 58 (26.2%) presented BKV-CH. In the group with BKV-CH, 39 (67.2%) were 18 years old or older, the median age was 30 years (range < 1 years – 73 years) and 41 (70.6%) were male. The most prevalent diagnosis was acute leukemia (AML 22%; ALL 37.9%). Most patients had high-relapse risk (65.5%). Cases of allo-HCST included matched related donors (20.6%), matched unrelated donors (58.6%) and haploidentical donors (20.6%). The stem cell source included umbilical cord blood cells (31%) and bone marrow cells (51.3%). Myeloablative was prevalent conditioning for BKV-CH patients (67,2%). At 1 year, the cumulative incidence of HC was 27% (95% CI 21%-33%). The 1-year incidence of CMV reactivation and acute GVHD II-IV in the group of HC-BKV was 57% [95% CI 44%-69%] and 54% [95% CI 40%-66%], respectively. In a multivariate analysis taking into account age, sex, risk of relapse, source of HSCs, intensity of conditioning, CMV reactivation and acute GVHD, use of TBI or Cy on conditioning and use of MMF or ATG for GVHD prophylaxis, only GVHD grade II-IV was associated with an increased incidence of HC-BKV (RR 3.34, 95% CI 1.76-6.37, p = 0.00). Patients who developed HC had an inferior OS (5 years: 24% vs. 50%; HR 3.81, CI 95% 2.49 – 5.83 p <0.000). In the multivariate Cox analysis for OS, development of HC-BKV (RR 3.54, 95% CI 2.25-5.56, p = 0.00) and CMV reactivation (SRR 1.85, 95% CI 1.19-2.90, p = 0.00) were associated with an increased mortality. Urinary catheterization and bladed irrigation were associated with decreased OS in patients with HC-BKV (OS in 5 year 14% [95% CI 5 – 26%] versus 44% [95% 20% – 65%], p < 0.02).
Conclusion: The development of HC-BKV was associated with an inferior OS in patients undergoing allo-HSCT. Even after adjusting for several variables, including development of acute GVHD and CMV reactivation, HC still remained an important factor associated with decreased survival.