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Viral Infections in Unrelated Allogeneic Stem Cell Transplantation with Post-Transplant Cyclophosphamide Compared with the Use of Thymoglobulin

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Introduction: The low rates of graft versus host disease (GVHD) and acceptable rates of survival with post-transplant cyclophosphamide (PTCy) in haploidential transplant (Haplo-HSCT) encouraged trials testing its use in HLA matched sibling and unrelated donor transplantation (UD-HSCT). A critical concern with its use is the increased immunosuppression leading to more infection complications. A recent trial comparing Haplo-HSCT and sibling transplant with PTCy and calcineurin inhibitor-based prophylaxis found higher rates of CMV DNAemia in the PTCy group.

Objective: To compare viral infections in patients undergoing UD-HSCT with PTCy to UD-HSCT with thymoglobulin (ATG).

Methodology: We analyzed 104 consecutive patients with hematological malignancies and aplastic anemia, who underwent UD-HSCT with ATG or PTCy, excluding a second allogeneic transplant, from 2010-2021. Viral monitoring with quantitative PCR for CMV and adenovirus were performed weekly, EBV every 14 days, and BK virus was performed in patients with haematuria. The event reactivation/viral infection was assessed in the first 6 months.

Results: In UD-HSCT with ATG group, there were 88 patients, the median age was 47 y/o and 73.8%, 23.8%, and 2.2% used myeloablative (MA), reduced intensity (RIC) and non-myeloablative regimen, respectively. Bone marrow graft was used in 50% of the cases. 85.2% were 10/10 matched. All patients received ATG 5mg/Kg, MTX and calcineurin inhibitor as immunosuppression. 89.7% of patients and 70.4% of donors were CMV serology positive.

In UD-HSCT with PTCy group, there were 16 patients, the median age was 40 y/o. 87.5% used MA and 12.5% RIC regimen. 62.5% used bone marrow (BM) source. All patients received MMF, tacrolimus, and PTCy 50mg/Kg D+3 and +4 and 87.5% were 10/10 matched. 93.7% of patients and 87.5% of donors were CMV serology positive.

The cumulative incidence of CMV reactivation was 69.3% with ATG and 75% with PTCy (p=0.08) (Figure 1), BKV hemorrhagic cystitis occurred in 22.9% with ATG and 14.2% with PTCy (p=0.46). Adenovirus reactivation occurred in 3.6% with ATG and 7.1% with PTCy (p=0.37) and Epstein Barr-Virus occurred in 18.4% with ATG and 0% with PTCy (p=0.09).

In the group of patients with CMV reactivation, the maximal viral load was 1601 (235-152,169) UI/ml in the ATG group and 1011 (326-2661) UI/ml in PTCy (p=0.17). Second CMV reactivation occurred in 18% in the ATG group and 6% in the PTCy (p=0.29). Disease caused by CMV occurred in 5.6% in ATG and 18.7% in PTCy (p=0.10).

Conclusion: The incidence of CMV reactivation was high, probably due to intense immunosuppression in both groups and high frequency of positive CMV serostatus. CMV and adenovirus reactivation was higher with PTCy and EBV was higher with ATG, although without statistically significant difference, probably because of relatively small number of patients in PTCy group. Further analyses with more patients are necessary.
Introduction: Infections remain a common cause of morbidity and mortality following hematopoietic stem cell transplant (HSCT). Pneumocystis jirovecii pneumonia (PJP) is an opportunistic infection that can occur in HSCT patients. The association is best demonstrated in allogeneic HSCT, occurring less commonly in autologous HSCT. However, reports on PJP incidence, timing of infection, and outcomes among autologous HSCT cohorts are limited. Furthermore, while current guidelines recommend 3-6 months of prophylaxis against PJP following autologous HSCT, the optimal duration and necessity of prophylaxis is not well established.

Objectives: This study aimed to characterize PJP incidence, timing, risk factors, mortality, and patterns of prophylaxis after autologous HSCT.

Methods: We performed a single-center retrospective analysis of autologous HSCT recipients over a 20-year period. The cohort consisted of a total of 2082 patients, 1221 male (58.6%), with median age 56 (range 10 months - 77 years, 91.2% ≥ 18 years). Cases of PJP occurring within 2 years of HSCT were identified, along with use of PJP prophylaxis over the 6-month period post-HSCT.

Results: Of the 2082 patients undergoing autologous HSCT, 704 patients (33.8%) received PJP prophylaxis in the first 6 months following transplant. Prophylaxis rates varied over time, ranging from 14.6% to 80.0% when calculated by year of transplant (Figure 1). Trimethoprim-sulfamethoxazole (TMP-SMX) was the most used prophylaxis agent (70.3%), followed by inhaled pentamidine (31.8%), with intravenous pentamidine (8.1%), dapsone (7.1%), and atovaquone (2.6%) being used less frequently. Patients often received multiple agents over the time period.

Conclusion: Our analysis reveals that among a large cohort, incidence of PJP following autologous HSCT is low. This was the case even with relatively modest rates of PJP prophylaxis in the first 6 months following transplant. Most cases of PJP occurred in patients receiving additional immunosuppression and rarely occurred in the first 3 months after transplant.

486

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