Activation Of Selected Opportunistic Viral Infections After Allogenic Stem Cell Transplant

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Introduction

Reactivation of latent viral infections in immunosuppressed hosts, remains a life-threatening complication in 38%-67% of recipients following allogenic stem cell transplantation (alloHSCT). Viral-induced endothelial damage, triggers pro-inflammatory cascades leading to adverse events. Moreover, viral-induced alternations of surface molecules involved in histocompatibility and cell adhesion, could result in development of acute and/or chronic graft-versus-host disease (GVHD) (1,2).

Aim of the Study

To determine relationships between selected pre-, peri- and post-transplant parameters, including non-relapse mortality (NRM), with activation of opportunistic viral infections after alloHSCT - Cytomegalovirus (CMV), Epstein-Barr virus (EBV), Human Herpetic virus 6 (HHV6) and Parvovirus B19 (PBV19)

Materials and Methodology

116 recipients underwent alloHSCT during the period 2011-2018. Patients had at least one positive DNA detection of the inspected viruses. Presence of viral DNA was assessed from a variety of tissue and specimen samples using real-time polymerase chain reaction (RT-PCR). Statistically analyses was perfomed using Kaplan-Meier method with Log-rank test (KM-LT) and Mann-Whitney U test (MWUT) as presented in Table 1.

Results

DNA detection in days post-transplant for CMV, HHV6 and PVB19 are 31 (range 3 - 692), 26 (range 2 - 698) and 33 (range 6 - 698), respectively. First EBV detection was observed significantly later (P = 0.002), at the median of 63 (range 15 - 848) post-transplant days *(Figure 1)*. ATG administration was the only factor associated with higher risk of CMV activation (P = 0.02) *(Figure 2)*. HHV6 was detected more frequently in the gastrointestinal tract *(Chart 1-4)*. Patients with HHV6 reactivation had higher risk of acute GVHD (P = 0.03) *(Figure 3)* and NRM (P = 0.01) *(Figure 4)*.

Table 1. **Statistical analyses**

Non-metric parameters analysed with probability of post-transplant survival without viral activation (KM-LT)	Viral activation impact on the probability of post-transplant survival without (MWUT):	Metric parameters analysed with post-transplant viral reactivation (KM-LT)
• Primary disease status at alloHSCT • Used donor • Conditioning regimen intensity • Antithymocyte globulin (ATG) administration in conditioning • Post-transplant immunosuppression intensity	• Acute GVHD (aGVHD) • Chronic GVHD (cGVHD) • NRM	• Mononuclear cells (MNC) in transfused graft • CD34+ in transfused graft • CD3+ in transfused graft • CD4+ in transfused graft • CD8+ in transfused graft

Chart 1. **PBV19 detection in selected specimens**

Chart 2. **HHV6 detection in selected specimens**

Chart 3. **CMV detection in selected specimens**

Chart 4. **EBV detection in selected specimens**

Figure 1. **Comparison of survival without viral detection**

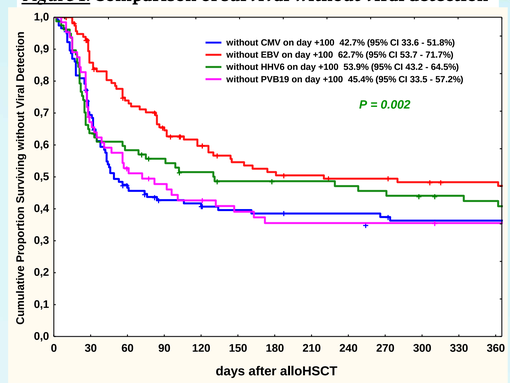


Figure 3: **HHV6 activation and survival without NRM**

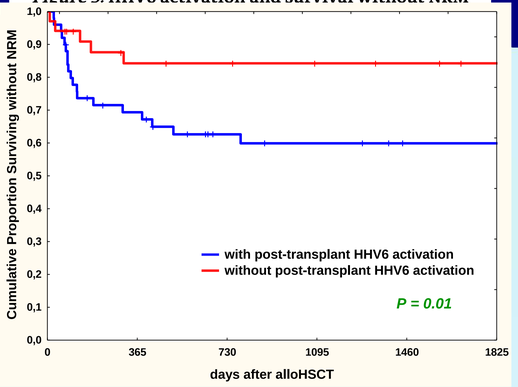


Figure 2. **ATG administration and survival without CMV detection**

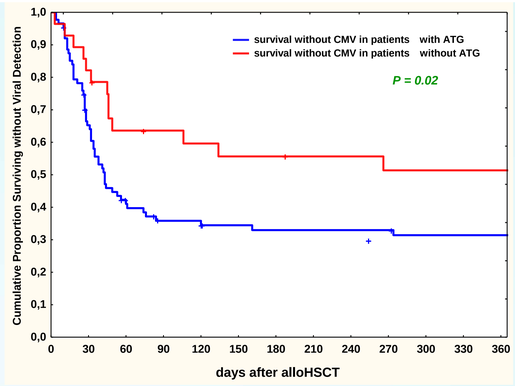
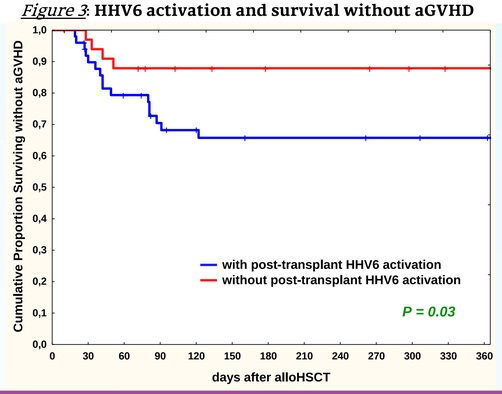


Figure 3: **HHV6 activation and survival without aGVHD**



Conclusion

Our analysis revealed that significant portion of viral DNA was detected in specimens other than plasma. Overall, EBV DNA detections were less frequent, and detected a month later, compared to other observed viral reactivations. Perhaps due to the intensified immunosuppressive treatment for aGVHD being the potential trigger (1,3). CMV-DNA detections were significantly more frequent in patients allografted after conditionings containing ATG, notably due to its T cell-depletion properties (1,4,5). Our findings also confirm the association of HHV6 and aGVHD, as the time of HHV6 DNA detection is concurrent with aGVHD, and also NRM events. HHV6 was detected frequently in gastrointestinal mucosa, which is postulated to be primarily involved in aGVHD development (1,5,6).

References

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