GENETIC VARIABILITY OF THE EPSTEIN-BARR VIRUS AND ITS RELATIONSHIP WITH POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDERS

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INTRODUCTION: Epstein Barr virus (EBV) infection in transplant patients is associated with the development of Post-transplant Lymphoproliferative Disorders (PTLD). Analysis of viral genetic variability could identify strains that contribute to the development of PTLD or only reflecting local geographic circulation. Our aim was to analyze the genetic diversity of EBV and its relationship with PTLD.

MATERIALS AND METHODS:

i) *Cross-sectional study*: Tonsils and peripheral blood mononuclear cells (PBMC) of 52 transplant recipients with PTLD (Tx-PTLD), 44 transplant recipients without PTLD (Tx) and 57 non-transplant patients (Non-Tx), were analyzed.

ii) *Exploratory study on the frequency of appearance of genetic variability*: PBMC taken during the follow-up of 12 transplant patients, 6 of whom developed PTLD, were studied.

EBV-1 and EBV-2 types and variants in EBNA-1 and LMP-1 were determined by PCR/sequencing. MEGA 5 software was used for phylogenetic analysis and WinPEPI 11.19 for statistical analysis.

RESULTS: In the cross-sectional study, the following were detected: 1) The EBV-1 and EBV-2 types, with a frequency of EBV-1 higher than 80% and a greater presence of co-infection in Tx and Tx-PTLD groups than in Non-Tx. 2) EBNA-1 variants in decreasing frequency: V-Leu, P-Thr, P-Ala and V-Ala in all groups. Four new subvariants were described. 3) Wide variability in LMP-1, being a variant of China-1 (China-1∗) the only one detected in Non-Tx and the predominant one in Tx and Tx-PTLD. There were no differences in the distribution of the viral types, nor in the EBNA-1 or LMP-1 variants among Tx-PTLD, Tx and Non-Tx groups ($p>0.05$), nor between the tonsils or PBMC samples ($p>0.05$).

In the exploratory study, the same EBV type and EBNA-1 variant were observed in Tx group (EBV-1 / EBNA-$1_{V\text{-}Leu\ Ag}$), while before or at the diagnosis of PTLD, the EBV-2 and/or EBNA-1_{PThr} were identified in all cases of Tx-PTLD .

CONCLUSIONS: The PTLD are not associated with an EBV specific variability pattern, although EBV-2 type or EBNA-$1_{P\text{-}Thr}$ variant could indicate a tendency for their development. In our region, the predominant viral type and variants in EBNA-1 and LMP-1 would be EBV-1, EBNA-$1_{V\text{-}Leu}$ and LMP-$1_{China\text{-}1}$∗, respectively.